## CLAIMS

We claim the following:

```
1
              A hematopoietic protein comprising; an amino acid sequence
2
    of the formula:
 3
               R_1-L_1-R_2, R_2-L_1-R_1, R_1-R_2, or R_2-R_1
 4
 5
6
         wherein R<sub>1</sub> and R<sub>2</sub> are independently selected from the
7
    group consisting of:
8
9
          (I) A polypeptide comprising a modified human G-CSF amino
10
    acid sequence selected from the group consisting of:
11
12
               (a) an amino acid sequence of the formula:
13
14
    Xaa Xaa Xaa Gly Pro Ala Ser Ser Leu Pro Gln Ser Xaa
15
16
17
                              20
18
    Leu Leu Xaa Xaa Kaa Glu Gln Val Xaa Lys Xaa Gln Gly Xaa Gly
19
20
         30
                                                    40
    Ala Xaa Leu Gln Glu Xaa Leu Xaa Ala Thr Tyr Lys Leu Xaa Xaa
21
22
23
                              50
24
    Xaa Glu Xaa Xaa Val Xaa Xaa Gly His Ser Xaa Gly Ile Pro Trp
25
26
         60
                                                    70
27
    Ala Pro Leu Ser Ser Xaa Pro Ser Xaa Ala Leu Xaa Leu Ala Gly
28
29
30
    Xaa Leu Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu
31
32
33
    Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu
34
35
                              110
36
    Xaa Thr Leu Gln Xaa Asp Val Ala Asp Phe Ala Xaa Thr Ile Trp
37
38
        120
                                                    130
39
    Gln Gln Met Glu Xaa Xaa Gly Met Ala Pro Ala Leu Gln Pro Thr
```

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40
41
                             140
42
    Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Xaa Gln Xaa Xaa Ala
43
44
                                                  160
45
    Gly Gly Val Leu Val Ala Ser Xaa Leu Gln Xaa Phe Leu Xaa Xaa
46
47
                             170
48
    Ser Tyr Arq Val Leu Xaa Xaa Leu Ala Gln Pro (SEQ ID NO:1)
49
50
    wherein
51
52
    Xaa at position 1 is Thr, Ser, Arg, Tyr or Gly;
53
    Xaa at position 2 is Pro or Leu;
54
    Xaa at position 3 is Leu, Arg, Tyr or Ser;
55
    Xaa at position 13 is Phe, Ser, His, Thr or Pro;
    Xaa at position 16 is Lys, Pro, Ser, Thr or His;
56
57
    Xaa at position 17 is Cys, Ser, Gly, Ala, Ile, Tyr or
58
         Arg;
59
    Xaa at position 18 is Leu, Thr, Pro, His, Ile or Cys;
60
    Xaa at position 22 is Arg, Tyr, Ser, Thr or Ala;
61
    Xaa at position 24 is Ile, Pro, Tyr or Leu;
62
    Xaa at position 27 is Asp, or Gly;
63
    Xaa at position 30 is Ala, Ile, Leu or Gly;
    Xaa at position 34 is Lys or Ser;
64
65
    Xaa at position 36 is Cys or Ser;
66
    Xaa at position 42 is Cys or Ser;
67
    Xaa at position 43 is His, Thr, Gly, Val, Lys, Trp, Ala,
68
         Arq, Cys, or Leu;
69
    Xaa at position 44 is Pro, Gly, Arg, Asp, Val, Ala, His,
70
         Trp, Gln, or Thr;
71
    Xaa at position 46 is Glu, Arg, Phe, Arg, Ile or Ala;
72
    Xaa at position 47 is Leu or Thr;
73
    Xaa at position 49 is Leu, Phe, Arg or Ser;
74
    Xaa at position 50 is Leu, Ile, His, Pro or Tyr;
75
    Xaa at position 54 is Leu or His;
76
    Xaa at position 64 is Cys or Ser;
77
    Xaa at position 67 is Gln, Lys, Leu or Cys;
    Xaa at position 70 is Gln, Pro, Leu, Arg or Ser;
78
79
    Xaa at position 74 is Cys or Ser;
80
    Xaa at position 104 is Asp, Gly or Val;
81
    Xaa at position 108 is Leu, Ala, Val, Arg, Trp, Gln or
82
         Gly;
83
    Xaa at position 115 is Thr, His, Leu or Ala;
84
    Xaa at position 120 is Gln, Gly, Arg, Lys or His
85
    Xaa at position 123 is Glu, Arg, Phe or Thr
86
    Xaa at position 144 is Phe, His, Arg, Pro, Leu, Gln or
```

```
87
          Glu:
88
     Xaa at position 146 is Arg or Gln;
89
     Xaa at position 147 is Arg or Gln;
90
     Xaa at position 156 is His, Gly or Ser;
91
     Xaa at position 159 is Ser, Arg, Thr, Tyr, Val or Gly;
92
     Xaa at position 162 is Glu, Leu, Gly or Trp;
     Xaa at position 163 is Val, Gly, Arg or Ala;
93
94
     Xaa at position 169 is Arg, Ser, Leu, Arg or Cys;
95
     Xaa at position 170 is His, Arg or Ser;
96
97
     wherein optionally 1-11 amino acids from the N-terminus and 1-
98
     5 from the C-terminus can optionally be deleted from said
99
     modified human G-CSF amino acid sequence; and
100
101
     wherein the N-terminus is joined to the C-terminus directly or
102
     through a linker capable of joining the N-terminus to the C-
103
     terminus and having new C- and N-termini at amino acids:
104
105
106
     38 - 39
                             62-63
                                                  123-124
107
     39 - 40
                             63-64
                                                  124-125
108
     40 - 41
                             64-65
                                                  125-126
109
     41-42
                             65-66
                                                 126-127
110
     42 - 43
                             66-67
                                                 128-129
111
     43 - 44
                             67-68
                                                 128-129
112
     45 - 46
                             68-69
                                                 129-130
113
     48 - 49
                             69-70
                                                 130-131
114
     49-50
                             70-71
                                                 131-132
115
     52-53
                             71-72
                                                 132-133
116
     53-54
                             91-92
                                                 133-134
117
     54 - 55
                             92-93
                                                 134-135
118
     55-56
                             93-94
                                                  135-136
119
     56-57
                             94 - 95
                                                 136-137
120
     57-58
                             95-96
                                                 137-138
121
     58-59
                             96-97
                                                  138-139
122
     59-60
                             97-98
                                                  139-140
123
     60-61
                             98 - 99
                                                  140 - 141
124
     61-62
                             99-100
                                                  141-142
125
                                                  or 142-143
126
                                                respectively; and
127
128
                (b) an amino acid sequence of the formula:
129
130
131
     Xaa Xaa Xaa Gly Pro Ala Ser Ser Leu Pro Gln Ser Xaa
132
```

```
133
                              20
134
     Leu Leu Xaa Xaa Xaa Glu Gln Val Xaa Lys Xaa Gln Gly Xaa Gly
135
136
         30
                                                    40
137
     Ala Xaa Leu Gln Glu Xaa Leu Xaa Ala Thr Tyr Lys Leu Xaa Xaa
138
139
                              50
140
     Xaa Glu Xaa Xaa Val Xaa Xaa Gly His Ser Xaa Gly Ile Pro Trp
141
142
         .60
                                                    70
143
     Ala Pro Leu Ser Ser Xaa Pro Ser Xaa Ala Leu Xaa Leu Ala Gly
144
145
146
     Xaa Leu Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu
147
148
         90
                                                    100
149
     Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu
150
151
                              110
152
     Xaa Thr Leu Gln Xaa Asp Val Ala Asp Phe Ala Xaa Thr Ile Trp
153
154
         120
                                                    130
155
     Gln Gln Met Glu Xaa Xaa Gly Met Ala Pro Ala Leu Gln Pro Thr
156
157
                              140
158
     Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Xaa Gln Xaa Xaa Ala
159
160
161
     Gly Gly Val Leu Val Ala Ser Xaa Leu Gln Xaa Phe Leu Xaa Xaa
162
163
                              170
164
     Ser Tyr Arg Val Leu Xaa Xaa Leu Ala Gln Pro (SEQ ID NO:1)
165
166
     wherein
167
168
     Xaa at position 1 is Thr, Ser, Arg, Tyr or Gly;
169
     Xaa at position 2 is Pro or Leu;
     Xaa at position 3 is Leu, Arg, Tyr or Ser;
170
171
     Xaa at position 13 is Phe, Ser, His, Thr or Pro;
172
     Xaa at position 16 is Lys, Pro, Ser, Thr or His;
173
     Xaa at position 17 is Cys, Ser, Gly, Ala, Ile, Tyr or
174
          Ara;
175
     Xaa at position 18 is Leu, Thr, Pro, His, Ile or Cys;
176
     Xaa at position 22 is Arg, Tyr, Ser, Thr or Ala;
177
     Xaa at position 24 is Ile, Pro, Tyr or Leu;
178
     Xaa at position 27 is Asp, or Gly;
179
     Xaa at position 30 is Ala, Ile, Leu or Gly;
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180
     Xaa at position 34 is Lys or Ser;
181
     Xaa at position 36 is Cys or Ser;
182
     Xaa at position 42 is Cys or Ser;
183
     Xaa at position 43 is His, Thr, Gly, Val, Lys, Trp, Ala,
184
          Arg, Cys, or Leu;
185
     Xaa at position 44 is Pro, Gly, Arg, Asp, Val, Ala, His,
186
          Trp, Gln, or Thr;
187
     Xaa at position 46 is Glu, Arg, Phe, Arg, Ile or Ala;
188
     Xaa at position 47 is Leu or Thr;
189
     Xaa at position 49 is Leu, Phe, Arg or Ser;
190
     Xaa at position 50 is Leu, Ile, His, Pro or Tyr;
191
     Xaa at position 54 is Leu or His;
192
     Xaa at position 64 is Cys or Ser;
193
     Xaa at position 67 is Gln, Lys, Leu or Cys;
194
     Xaa at position 70 is Gln, Pro, Leu, Arg or Ser;
195
     Xaa at position 74 is Cys or Ser;
196
     Xaa at position 104 is Asp, Gly or Val;
197
     Xaa at position 108 is Leu, Ala, Val, Arg, Trp, Gln or
198
          Glv:
199
     Xaa at position 115 is Thr, His, Leu or Ala;
200
     Xaa at position 120 is Gln, Gly, Arg, Lys or His
201
     Xaa at position 123 is Glu, Arg, Phe or Thr
202
     Xaa at position 144 is Phe, His, Arg, Pro, Leu, Gln or
203
          Glu;
204
     Xaa at position 146 is Arg or Gln;
     Xaa at position 147 is Arg or Gln;
205
206
     Xaa at position 156 is His, Gly or Ser;
207
     Xaa at position 159 is Ser, Arg, Thr, Tyr, Val or Gly;
208
     Xaa at position 162 is Glu, Leu, Gly or Trp;
209
     Xaa at position 163 is Val, Gly, Arg or Ala;
     Xaa at position 169 is Arg, Ser, Leu, Arg or Cys;
210
211
     Xaa at position 170 is His, Arg or Ser,
212
213
214
     wherein optionally 1-11 amino acids from the N-terminus and 1-
215
     5 from the C-terminus can be deleted;
216
217
     wherein the N-terminus is joined to the C-terminus directly or
218
     through a linker capable of joining the N-terminus to the C-
219
     terminus and having new C- and N-terminus at amino acids:
220
221
     2-3
222
     10-11
223
     12-13
224
     18 - 19
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225
   122-123
226
   158-159
227
   169-170;
228
229
      (II) A polypeptide comprising; a modified human IL-3
230
   amino acid sequence of the formula:
231
232
233
   Ala Pro Met Thr Gln Thr Thr Ser Leu Lys Thr Ser Trp Val Asn
234
   1
             5
                          10
                                      15
235
236
   237
             20
                          25
                                      30
238
239
   Xaa Xaa Xaa Xaa Xaa Xaa Xaa Asn Xaa Xaa Xaa Xaa Xaa
240
             35
                          40
                                      45
241
242
   243
             50
                          55
                                      60
244
245
   246
             65
                          70
                                      75
247
248
   249
             80
                          85
                                      90
250
251
   252
             95
                          100
                                      105
253
254
   255
             110
                          115
                                      120
256
257
   Xaa Xaa Xaa Gln Gln Thr Thr Leu Ser Leu Ala Ile Phe
258
             125
                          130
                             (SEQ ID NO:2)
259
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260 wherein Xaa at position 17 is Ser, Lys, Gly, Asp, Met, Gln, or 261 262 Xaa at position 18 is Asn, His, Leu, Ile, Phe, Arg, or Gln; 263 Xaa at position 19 is Met, Phe, Ile, Arg, Gly, Ala, or Cys; 264 Xaa at position 20 is Ile, Cys, Gln, Glu, Arg, Pro, or Ala; 265 Xaa at position 21 is Asp, Phe, Lys, Arg, Ala, Gly, Glu, Gln, 266 Asn, Thr, Ser or Val; Xaa at position 22 is Glu, Trp, Pro, Ser, Ala, His, Asp, Asn, 267 268 Gln, Leu, Val or Gly; 269 Xaa at position 23 is Ile, Val, Ala, Gly, Trp, Lys, Phe, 270 Leu, Ser, or Arg; 271 Xaa at position 24 is Ile, Gly, Val, Arg, Ser, Phe, or Leu; Xaa at position 25 is Thr, His, Gly, Gln, Arg, Pro, or Ala; 272 273 Xaa at position 26 is His, Thr, Phe, Gly, Arg, Ala, or Trp; 274 Xaa at position 27 is Leu, Gly, Arg, Thr, Ser, or Ala; 275 Xaa at position 28 is Lys, Arg, Leu, Gln, Gly, Pro, Val or 276 277 Xaa at position 29 is Gln, Asn, Leu, Pro, Arg, or Val; 278 Xaa at position 30 is Pro, His, Thr, Gly, Asp, Gln, Ser, Leu, 279 or Lys; Xaa at position 31 is Pro, Asp, Gly, Ala, Arg, Leu, or Gln; 280 281 Xaa at position 32 is Leu, Val, Arg, Gln, Asn, Gly, Ala, or 282 Glu; 283 Xaa at position 33 is Pro, Leu, Gln, Ala, Thr, or Glu; 284 Xaa at position 34 is Leu, Val, Gly, Ser, Lys, Glu, Gln, Thr, 285 Arg, Ala, Phe, Ile or Met; 286 Xaa at position 35 is Leu, Ala, Gly, Asn, Pro, Gln, or Val; 287 Xaa at position 36 is Asp, Leu, or Val; 288 Xaa at position 37 is Phe, Ser, Pro, Trp, or Ile; 289 Xaa at position 38 is Asn, or Ala; 290 Xaa at position 40 is Leu, Trp, or Arg; 291 Xaa at position 41 is Asn, Cys, Arg, Leu, His, Met, or Pro; 292 Xaa at position 42 is Gly, Asp, Ser, Cys, Asn, Lys, Thr, Leu, 293 Val, Glu, Phe, Tyr, Ile, Met or Ala; 294 Xaa at position 43 is Glu, Asn, Tyr, Leu, Phe, Asp, Ala, Cys, 295 Gln, Arg, Thr, Gly or Ser;

296 Xaa at position 44 is Asp, Ser, Leu, Arg, Lys, Thr, Met, Trp, 297 Glu, Asn, Gln, Ala or Pro; 298 Xaa at position 45 is Gln, Pro, Phe, Val, Met, Leu, Thr, Lys, 299 Trp, Asp, Asn, Arg, Ser, Ala, Ile, Glu or His; 300 Xaa at position 46 is Asp, Phe, Ser, Thr, Cys, Glu, Asn, Gln, 301 Lys, His, Ala, Tyr, Ile, Val or Gly; 302 Xaa at position 47 is Ile, Gly, Val, Ser, Arg, Pro, or His; 303 Xaa at position 48 is Leu, Ser, Cys, Arg, Ile, His, Phe, Glu, 304 Lys, Thr, Ala, Met, Val or Asn; 305 Xaa at position 49 is Met, Arg, Ala, Gly, Pro, Asn, His, or 306 Asp; 307 Xaa at position 50 is Glu, Leu, Thr, Asp, Tyr, Lys, Asn, Ser, 308 Ala, Ile, Val, His, Phe, Met or Gln; 309 Xaa at position 51 is Asn, Arg, Met, Pro, Ser, Thr, or His; 310 Xaa at position 52 is Asn, His, Arg, Leu, Gly, Ser, or Thr; 311 Xaa at position 53 is Leu, Thr, Ala, Gly, Glu, Pro, Lys, Ser, 312 or Met; 313 Xaa at position 54 is Arg, Asp, Ile, Ser, Val, Thr, Gln, Asn, 314 Lys, His, Ala or Leu; 315 Xaa at position 55 is Arg, Thr, Val, Ser, Leu, or Gly; 316 Xaa at position 56 is Pro, Gly, Cys, Ser, Gln, Glu, Arg, His, 317 Thr, Ala, Tyr, Phe, Leu, Val or Lys; 318 Xaa at position 57 is Asn or Gly; 319 Xaa at position 58 is Leu, Ser, Asp, Arg, Gln, Val, or Cys; Xaa at position 59 is Glu Tyr, His, Leu, Pro, or Arg; 320 321 Xaa at position 60 is Ala, Ser, Pro, Tyr, Asn, or Thr; 322 Xaa at position 61 is Phe, Asn, Glu, Pro, Lys, Arg, or Ser; 323 Xaa at position 62 is Asn, His, Val, Arq, Pro, Thr, Asp, or 324 Ile; 325 Xaa at position 63 is Arg, Tyr, Trp, Lys, Ser, His, Pro, or 326 Val: 327 Xaa at position 64 is Ala, Asn, Pro, Ser, or Lys; 328 Xaa at position 65 is Val, Thr, Pro, His, Leu, Phe, or Ser; 329 Xaa at position 66 is Lys, Ile, Arg, Val, Asn, Glu, or Ser; 330 Xaa at position 67 is Ser, Ala, Phe, Val, Gly, Asn, Ile, Pro,

331

or

332 His; 333 Xaa at position 68 is Leu, Val, Trp, Ser, Ile, Phe, Thr, or 334 His: Xaa at position 69 is Gln, Ala, Pro, Thr, Glu, Arg, Trp, Gly, 335 336 or Leu; 337 Xaa at position 70 is Asn, Leu, Val, Trp, Pro, or Ala; Xaa at position 71 is Ala, Met, Leu, Pro, Arg, Glu, Thr, Gln, 338 339 Trp, or Asn; 340 Xaa at position 72 is Ser, Glu, Met, Ala, His, Asn, Arg, or 341 Asp; 342 Xaa at position 73 is Ala, Glu, Asp, Leu, Ser, Gly, Thr, or 343 344 Xaa at position 74 is Ile, Met, Thr, Pro, Arg, Gly, Ala; Xaa at position 75 is Glu, Lys, Gly, Asp, Pro, Trp, Arg, Ser, 345 346 Gln, or Leu; 347 Xaa at position 76 is Ser, Val, Ala, Asn, Trp, Glu, Pro, Gly, 348 349 Asp; 350 Xaa at position 77 is Ile, Ser, Arg, Thr, or Leu; 351 Xaa at position 78 is Leu, Ala, Ser, Glu, Phe, Gly, or Arg; 352 Xaa at position 79 is Lys, Thr, Asn, Met, Arg, Ile, Gly, or 353 354 Xaa at position 80 is Asn, Trp, Val, Gly, Thr, Leu, Glu, or 355 Arg; 356 Xaa at position 81 is Leu, Gln, Gly, Ala, Trp, Arg, Val, or 357 Lys; 358 Xaa at position 82 is Leu, Gln, Lys, Trp, Arq, Asp, Glu, Asn, 359 His, Thr, Ser, Ala, Tyr, Phe, Ile, Met or Val; 360 Xaa at position 83 is Pro, Ala, Thr, Trp, Arq, or Met; 361 Xaa at position 84 is Cys, Glu, Gly, Arg, Met, or Val; 362 Xaa at position 85 is Leu, Asn, Val, or Gln; 363 Xaa at position 86 is Pro, Cys, Arg, Ala, or Lys; 364 Xaa at position 87 is Leu, Ser, Trp, or Gly; 365 Xaa at position 88 is Ala, Lys, Arg, Val, or Trp; 366 Xaa at position 89 is Thr, Asp, Cys, Leu, Val, Glu, His, Asn, 367 or Ser;

368 Xaa at position 90 is Ala, Pro, Ser, Thr, Gly, Asp, Ile, or 369 Met: 370 Xaa at position 91 is Ala, Pro, Ser, Thr, Phe, Leu, Asp, or 371 His; 372 Xaa at position 92 is Pro, Phe, Arg, Ser, Lys, His, Ala, Gly, 373 Ile or Leu; 374 Xaa at position 93 is Thr, Asp, Ser, Asn, Pro, Ala, Leu, or 375 Arq; 376 Xaa at position 94 is Arg, Ile, Ser, Glu, Leu, Val, Gln, Lys, 377 His, Ala, or Pro; 378 Xaa at position 95 is His, Gln, Pro, Arg, Val, Leu, Gly, Thr, 379 Asn, Lys, Ser, Ala, Trp, Phe, Ile, or Tyr; 380 Xaa at position 96 is Pro, Lys, Tyr, Gly, Ile, or Thr; 381 Xaa at position 97 is Ile, Val, Lys, Ala, or Asn; 382 Xaa at position 98 is His, Ile, Asn, Leu, Asp, Ala, Thr, 383 Glu, Gln, Ser, Phe, Met, Val, Lys, Arg, Tyr or Pro; 384 Xaa at position 99 is Ile, Leu, Arg, Asp, Val, Pro, Gln, 385 Gly, Ser, Phe, or His; 386 Xaa at position 100 is Lys, Tyr, Leu, His, Arg, Ile, Ser, Gln, 387 or Pro; 388 Xaa at position 101 is Asp, Pro, Met, Lys, His, Thr, Val, 389 Tyr, Glu, Asn, Ser, Ala, Gly, Ile, Leu, or Gln; 390 Xaa at position 102 is Gly, Leu, Glu, Lys, Ser, Tyr, or Pro; 391 Xaa at position 103 is Asp, or Ser; 392 Xaa at position 104 is Trp, Val, Cys, Tyr, Thr, Met, Pro, Leu, 393 Gln, Lys, Ala, Phe, or Gly; 394 Xaa at position 105 is Asn, Pro, Ala, Phe, Ser, Trp, Gln, Tyr, 395 Leu, Lys, Ile, Asp, or His; 396 Xaa at position 106 is Glu, Ser, Ala, Lys, Thr, Ile, Gly, or 397 Pro; 398 Xaa at position 108 is Arg, Lys, Asp, Leu, Thr, Ile, Gln, His, 399 Ser, Ala or Pro; 400 Xaa at position 109 is Arg, Thr, Pro, Glu, Tyr, Leu, Ser, or 401 Gly;

Xaa at position 110 is Lys, Ala, Asn, Thr, Leu, Arg, Gln, His,

402 403

Glu, Ser, or Trp;

- 404 Xaa at position 111 is Leu, Ile, Arg, Asp, or Met; 405 Xaa at position 112 is Thr, Val, Gln, Tyr, Glu, His, Ser, or 406 Phe; 407 Xaa at position 113 is Phe, Ser, Cys, His, Gly, Trp, Tyr, Asp, 408 Lys, Leu, Ile, Val or Asn; 409 Xaa at position 114 is Tyr, Cys, His, Ser, Trp, Arg, or Leu; 410 Xaa at position 115 is Leu, Asn, Val, Pro, Arg, Ala, His, Thr, 411 Trp, or Met; 412 Xaa at position 116 is Lys, Leu, Pro, Thr, Met, Asp, Val, Glu, 413 Arg, Trp, Ser, Asn, His, Ala, Tyr, Phe, Gln, or Ile; 414 Xaa at position 117 is Thr, Ser, Asn, Ile, Trp, Lys, or Pro; 415 Xaa at position 118 is Leu, Ser, Pro, Ala, Glu, Cys, Asp, or 416 Tyr; 417 Xaa at position 119 is Glu, Ser, Lys, Pro, Leu, Thr, Tyr, or 418 Arq; 419 Xaa at position 120 is Asn, Ala, Pro, Leu, His, Val, or Gln; 420 Xaa at position 121 is Ala, Ser, Ile, Asn, Pro, Lys, Asp, or 421 Gly; 422 Xaa at position 122 is Gln, Ser, Met, Trp, Arg, Phe, Pro, His, 423 Ile, Tyr, or Cys; 424 Xaa at position 123 is Ala, Met, Glu, His, Ser, Pro, Tyr, or 425 Leu; 426 427 wherein from 1 to 14 amino acids can optionally be deleted 428 from the N-terminus and/or from 1 to 15 amino acids can 429 optionally be deleted from the C-terminus of said modified 430 human IL-3 amino acid sequence; wherein from 0 to 44 of the 431 amino acids designated by Xaa are different from the 432 corresponding amino acids of native (1-133) human interleukin-433 3; and 434
- 437 438

436

wherein the N-terminus is joined to the C-terminus directly or

the C-terminus and having new C- and N-termini at amino acids:

through a linker  $(L_2)$ , capable of joining the N-terminus to

26-27	49-50	83-84
27-28	50-51	84-85
28-29	51-52	85-86
29-30	52-53	86-87
30-31	53-54	87-88
31-32	54-55	88-89
32-33	64-65	89-90
33-34	65-66	90-91
34-35	66-67	91-92
35-36	67-68	92-93
36-37	68-69	97-98
37-38	69-70	98-99
38-39	70-71	99-100
39-40	71-72	100-101
40-41	72-73	101-102
41-42	82-83	102-103
		or 103-104
		respectively;

(III) A polypeptide comprising; a modified human c-mpl ligand amino acid sequence selected from the group consisiting of:

(a) an amino acid sequence of the formula:

 ${\tt SerProAlaProProAlaCysAspLeuArgValLeuSerLysLeuLeuArgAspSer}$ 

HisValLeuHisSerArgLeuSerGlnCysProGluValHisProLeuProThrPro 

ValLeuLeuProAlaValAspPheSerLeuGlyGluTrpLysThrGlnMetGluGlu 

ThrLysAlaGlnAspIleLeuGlyAlaValThrLeuLeuGluGlyValMetAla 

AlaArgGlyGlnLeuGlyProThrCysLeuSerSerLeuLeuGlyGlnLeuSerGly 8.5 

GlnValArgLeuLeuGlyAlaLeuGlnSerLeuLeuGlyThrGlnXaaXaaXaa 

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464
465
     XaaGlyArgThrThrAlaHisLysAspProAsnAlaIlePheLeuSerPheGlnHis
     115
466
                    120
                                    125
                                                    130
467
468
     LeuLeuArgGlyLysValArgPheLeuMetLeuValGlyGlySerThrLeuCysVal
469
                        140
470
471
     Arg (SEQ ID NO:256)
472
     153
473
474
     wherein
475
476
     Xaa at position 112 is deleted or Leu, Ala, Val, Ile,
477
     Phe, Trp, or Met;
478
     Xaa at position 113 is deleted or Pro, Phe, Ala, Val,
                                                              Leu,
479
     Ile, Trp, or Met;
480
     Xaa at position 114 is deleted or Pro, Phe, Ala, Val,
481
     Ile, Trp, or Met;
482
     Xaa at position 115 is deleted or Gln, Gly, Ser, Thr,
483
     Asn; and
484
485
     wherein the N-terminus is joined to the C-terminus directly or
486
     through a linker (L2) capable of joining the N-terminus to the
487
     C-terminus and having new C- and N-termini at amino acids:
```

26-27	51-52	108-109
27-28	52-53	109-110
28-29	53-54	110-111
29-30	54-55	111-112
30-31	55-56	112-113
32-33	56-57	113-114
33-34	57-58	114-115
34-35	58-59	115-116
36-37	59-60	116-117
37-38	78-79	117-118
38-39	79-80	118-119
40-41	80-81	119-120
41-42	81-82	120-121
42-43	82-83	121-122
43-44	83-84	122-123
44-45	84-85	123-124

46-47	85-86	124-125
47-48	86-87	125-126
48-49	87-88	126-127
50-51	88-89	or 127-128
		respectively; and

(b) an amino acid sequence of the formula:

491 492

SerProAlaProProAlaXaaAspLeuArgValLeuSerLysLeuLeuArgAspSer 1 5 10 15

493 494 495

496

HisValLeuHisSerArgLeuSerGlnCysProGluValHisProLeuProThrPro 20 25 30 35

497 498

ValLeuLeuProAlaValAspPheSerLeuGlyGluTrpLysThrGlnMetGluGlu 40 45 50 55

499500501

ThrLysAlaGlnAspIleLeuGlyAlaValThrLeuLeuLeuGluGlyValMetAla 60 65 70 75

502503504

AlaArgGlyGlnLeuGlyProThrCysLeuSerSerLeuLeuGlyGlnLeuSerGly
80 85 90 95

505506507

GlnValArgLeuLeuGlyAlaLeuGlnSerLeuLeuGlyThrGlnXaaXaaXaa

508 509 510

XaaGlyArgThrThrAlaHisLysAspProAsnAlaIlePheLeuSerPheGlnHis 115 120 125 130

511512513

LeuLeuArgGlyLysValArgPheLeuMetLeuValGlyGlySerThrLeuXaaVal 135 140 145 150

514515

516 Arg (SEQ ID NO:283)

**517** 153

518

519 wherein

520 Xaa at position 7 is Ser or Ala;

521 Xaa at position 112 is deleted or Leu, Ala, Val, Ile,

Pro, Phe, Trp, or Met;

523 Xaa at position 113 is deleted or Pro, Phe, Ala, Val,

Leu, Ile, Trp, or Met;

525 Xaa at position 114 is deleted or Pro, Phe, Ala, Val,

Leu, Ile, Trp, or Met;

527 Xaa at position 115 is deleted or Gln, Gly, Ser, Thr,

528 Tyr, or Asn;

529 Xaa at position 151 is Ser or Ala,

530531

532

533

wherein the N-terminus is joined to the C-terminus directly or through a linker capable of joining the N-terminus to the Cterminus and having new C- and N-termini at amino acids:

534

26-27	51-52	108-109
27-28	52-53	109-110
28-29	53-54	110-111
29-30	54-55	111-112
30-31	55-56	112-113
32-33	56-57	113-114
33-34	57-58	114-115
34-35	58-59	115-116
36-37	59-60	116-117
37-38	78-79	117-118
38-39	79-80	118-119
40-41	80-81	119-120
41-42	81-82	120-121
42-43	82-83	121-122
43-44	83-84	122-123
44-45	84-85	123-124
46-47	85-86	124-125
47-48	86-87	125-126
48-49	87-88	126-127
50-51	88-89	or 127-128;

535536

(IV) A polypeptide comprising; a modified human IL-3 amino acid sequence of the formula:

537538

539	Ala	Pro	Met	Thr	Gln	Thr	Thr	Ser	Leu	Lys	Thr	Ser	Trp	Val	Asn
540	1				5					10					15

541

542	Cys	Xaa													
543					20					25					30

544545

546

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Asn Xaa Xaa Xaa Xaa Xaa Asa 35 40 45

```
547
548
    549
                 50
                                 55
                                                  60
550
551
    552
                 65
                                 70
                                                  75
553
554
    555
                                 85
                 80
                                                  90
556
557
    558
                 95
                                 100
                                                  105
559
560
    561
                 110
                                 115
                                                  120
562
563
    Xaa Xaa Xaa Gln Gln Thr Thr Leu Ser Leu Ala Ile Phe
564
                 125
                                 130 (SEO ID NO:2)
565
    wherein Xaa at position 17 is Ser, Lys, Gly, Asp, Met, Gln, or
566
567
    Arg;
568
    Xaa at position 18 is Asn, His, Leu, Ile, Phe, Arg, or Gln;
569
    Xaa at position 19 is Met, Phe, Ile, Arg, Gly, Ala, or Cys;
570
    Xaa at position 20 is Ile, Cys, Gln, Glu, Arg, Pro, or Ala;
571
    Xaa at position 21 is Asp, Phe, Lys, Arg, Ala, Gly, Glu, Gln,
572
    Asn, Thr, Ser or Val;
573
    Xaa at position 22 is Glu, Trp, Pro, Ser, Ala, His, Asp, Asn,
574
    Gln, Leu, Val or Gly;
575
    Xaa at position 23 is Ile, Val, Ala, Gly, Trp, Lys, Phe,
576
        Leu, Ser, or Arg;
577
    Xaa at position 24 is Ile, Gly, Val, Arg, Ser, Phe, or Leu;
578
    Xaa at position 25 is Thr, His, Gly, Gln, Arg, Pro, or Ala;
579
    Xaa at position 26 is His, Thr, Phe, Gly, Arg, Ala, or Trp;
580
    Xaa at position 27 is Leu, Gly, Arg, Thr, Ser, or Ala;
581
    Xaa at position 28 is Lys, Arg, Leu, Gln, Gly, Pro, Val or
582
    Trp;
```

583 Xaa at position 29 is Gln, Asn, Leu, Pro, Arg, or Val; 584 Xaa at position 30 is Pro, His, Thr, Gly, Asp, Gln, Ser, Leu, 585 or Lys; 586 Xaa at position 31 is Pro, Asp, Gly, Ala, Arg, Leu, or Gln; 587 Xaa at position 32 is Leu, Val, Arg, Gln, Asn, Gly, Ala, or 588 Glu; 589 Xaa at position 33 is Pro, Leu, Gln, Ala, Thr, or Glu; 590 Xaa at position 34 is Leu, Val, Gly, Ser, Lys, Glu, Gln, Thr, 591 Arg, Ala, Phe, Ile or Met; 592 Xaa at position 35 is Leu, Ala, Gly, Asn, Pro, Gln, or Val; 593 Xaa at position 36 is Asp, Leu, or Val; 594 Xaa at position 37 is Phe, Ser, Pro, Trp, or Ile; 595 Xaa at position 38 is Asn, or Ala; Xaa at position 40 is Leu, Trp, or Arg; 596 597 Xaa at position 41 is Asn, Cys, Arg, Leu, His, Met, or Pro; 598 Xaa at position 42 is Gly, Asp, Ser, Cys, Asn, Lys, Thr, Leu, 599 Val, Glu, Phe, Tyr, Ile, Met or Ala; Xaa at position 43 is Glu, Asn, Tyr, Leu, Phe, Asp, Ala, Cys, 600 601 Gln, Arg, Thr, Gly or Ser; Xaa at position 44 is Asp, Ser, Leu, Arg, Lys, Thr, Met, Trp, 602 603 Glu, Asn, Gln, Ala or Pro; 604 Xaa at position 45 is Gln, Pro, Phe, Val, Met, Leu, Thr, Lys, 605 Trp, Asp, Asn, Arg, Ser, Ala, Ile, Glu or His; 606 Xaa at position 46 is Asp, Phe, Ser, Thr, Cys, Glu, Asn, Gln, 607 Lys, His, Ala, Tyr, Ile, Val or Gly; 608 Xaa at position 47 is Ile, Gly, Val, Ser, Arg, Pro, or His; 609 Xaa at position 48 is Leu, Ser, Cys, Arg, Ile, His, Phe, Glu, 610 Lys, Thr, Ala, Met, Val or Asn; 611 Xaa at position 49 is Met, Arg, Ala, Gly, Pro, Asn, His, or 612 Asp; 613 Xaa at position 50 is Glu, Leu, Thr, Asp, Tyr, Lys, Asn, Ser, 614 Ala, Ile, Val, His, Phe, Met or Gln; Xaa at position 51 is Asn, Arg, Met, Pro, Ser, Thr, or His; 615 616 Xaa at position 52 is Asn, His, Arg, Leu, Gly, Ser, or Thr; 617 Xaa at position 53 is Leu, Thr, Ala, Gly, Glu, Pro, Lys, Ser,

618

or Met;

654

or

Asp;

619 Xaa at position 54 is Arg, Asp, Ile, Ser, Val, Thr, Gln, Asn, 620 Lys, His, Ala or Leu; 621 Xaa at position 55 is Arg, Thr, Val, Ser, Leu, or Gly; 622 Xaa at position 56 is Pro, Gly, Cys, Ser, Gln, Glu, Arg, His, 623 Thr, Ala, Tyr, Phe, Leu, Val or Lys; 624 Xaa at position 57 is Asn or Gly; 625 Xaa at position 58 is Leu, Ser, Asp, Arg, Gln, Val, or Cys; 626 Xaa at position 59 is Glu Tyr, His, Leu, Pro, or Arg; 627 Xaa at position 60 is Ala, Ser, Pro, Tyr, Asn, or Thr; 628 Xaa at position 61 is Phe, Asn, Glu, Pro, Lys, Arg, or Ser; 629 Xaa at position 62 is Asn, His, Val, Arg, Pro, Thr, Asp, or 630 Ile; 631 Xaa at position 63 is Arg, Tyr, Trp, Lys, Ser, His, Pro, or 632 Val; 633 Xaa at position 64 is Ala, Asn, Pro, Ser, or Lys; 634 Xaa at position 65 is Val, Thr, Pro, His, Leu, Phe, or Ser; Xaa at position 66 is Lys, Ile, Arg, Val, Asn, Glu, or Ser; 635 636 Xaa at position 67 is Ser, Ala, Phe, Val, Gly, Asn, Ile, Pro, 637 or His; 638 Xaa at position 68 is Leu, Val, Trp, Ser, Ile, Phe, Thr, or 639 640 Xaa at position 69 is Gln, Ala, Pro, Thr, Glu, Arg, Trp, Gly, 641 or Leu; 642 Xaa at position 70 is Asn, Leu, Val, Trp, Pro, or Ala; 643 Xaa at position 71 is Ala, Met, Leu, Pro, Arg, Glu, Thr, Gln, 644 Trp, or Asn; 645 Xaa at position 72 is Ser, Glu, Met, Ala, His, Asn, Arg, or 646 Asp; 647 Xaa at position 73 is Ala, Glu, Asp, Leu, Ser, Gly, Thr, or 648 Arg; 649 Xaa at position 74 is Ile, Met, Thr, Pro, Arg, Gly, Ala; 650 Xaa at position 75 is Glu, Lys, Gly, Asp, Pro, Trp, Arq, Ser, 651 Gln, or Leu; 652 Xaa at position 76 is Ser, Val, Ala, Asn, Trp, Glu, Pro, Gly,

655 Xaa at position 77 is Ile, Ser, Arg, Thr, or Leu; 656 Xaa at position 78 is Leu, Ala, Ser, Glu, Phe, Gly, or Arg; 657 Xaa at position 79 is Lys, Thr, Asn, Met, Arq, Ile, Gly, or 658 Asp; 659 Xaa at position 80 is Asn, Trp, Val, Gly, Thr, Leu, Glu, or 660 661 Xaa at position 81 is Leu, Gln, Gly, Ala, Trp, Arg, Val, or 662 Lys; Xaa at position 82 is Leu, Gln, Lys, Trp, Arg, Asp, Glu, Asn, 663 664 His, Thr, Ser, Ala, Tyr, Phe, Ile, Met or Val; 665 Xaa at position 83 is Pro, Ala, Thr, Trp, Arg, or Met; 666 Xaa at position 84 is Cys, Glu, Gly, Arq, Met, or Val; 667 Xaa at position 85 is Leu, Asn, Val, or Gln; 668 Xaa at position 86 is Pro, Cys, Arg, Ala, or Lys; 669 Xaa at position 87 is Leu, Ser, Trp, or Gly; 670 Xaa at position 88 is Ala, Lys, Arg, Val, or Trp; 671 Xaa at position 89 is Thr, Asp, Cys, Leu, Val, Glu, His, Asn, 672 or Ser; 673 Xaa at position 90 is Ala, Pro, Ser, Thr, Gly, Asp, Ile, or 674 Met; 675 Xaa at position 91 is Ala, Pro, Ser, Thr, Phe, Leu, Asp, or 676 677 Xaa at position 92 is Pro, Phe, Arg, Ser, Lys, His, Ala, Gly, 678 Ile or Leu; Xaa at position 93 is Thr, Asp, Ser, Asn, Pro, Ala, Leu, or 679 680 Arg; 681 Xaa at position 94 is Arg, Ile, Ser, Glu, Leu, Val, Gln, Lys, 682 His, Ala, or Pro; Xaa at position 95 is His, Gln, Pro, Arg, Val, Leu, Gly, Thr, 683 684 Asn, Lys, Ser, Ala, Trp, Phe, Ile, or Tyr; 685 Xaa at position 96 is Pro, Lys, Tyr, Gly, Ile, or Thr; 686 Xaa at position 97 is Ile, Val, Lys, Ala, or Asn; 687 Xaa at position 98 is His, Ile, Asn, Leu, Asp, Ala, Thr, 688 Glu, Gln, Ser, Phe, Met, Val, Lys, Arg, Tyr or Pro; Xaa at position 99 is Ile, Leu, Arg, Asp, Val, Pro, Gln, 689 690 Gly, Ser, Phe, or His;

726

Gly;

691 Xaa at position 100 is Lys, Tyr, Leu, His, Arg, Ile, Ser, Gln, 692 or Pro; 693 Xaa at position 101 is Asp, Pro, Met, Lys, His, Thr, Val, 694 Tyr, Glu, Asn, Ser, Ala, Gly, Ile, Leu, or Gln; 695 Xaa at position 102 is Gly, Leu, Glu, Lys, Ser, Tyr, or Pro; 696 Xaa at position 103 is Asp, or Ser; 697 Xaa at position 104 is Trp, Val, Cys, Tyr, Thr, Met, Pro, Leu, 698 Gln, Lys, Ala, Phe, or Gly; 699 Xaa at position 105 is Asn, Pro, Ala, Phe, Ser, Trp, Gln, Tyr, 700 Leu, Lys, Ile, Asp, or His; 701 Xaa at position 106 is Glu, Ser, Ala, Lys, Thr, Ile, Gly, or 702 703 Xaa at position 108 is Arg, Lys, Asp, Leu, Thr, Ile, Gln, His, 704 Ser, Ala or Pro; 705 Xaa at position 109 is Arg, Thr, Pro, Glu, Tyr, Leu, Ser, or 706 Gly; 707 Xaa at position 110 is Lys, Ala, Asn, Thr, Leu, Arg, Gln, His, 708 Glu, Ser, or Trp; 709 Xaa at position 111 is Leu, Ile, Arg, Asp, or Met; 710 Xaa at position 112 is Thr, Val, Gln, Tyr, Glu, His, Ser, or 711 Phe; 712 Xaa at position 113 is Phe, Ser, Cys, His, Gly, Trp, Tyr, Asp, 713 Lys, Leu, Ile, Val or Asn; 714 Xaa at position 114 is Tyr, Cys, His, Ser, Trp, Arg, or Leu; 715 Xaa at position 115 is Leu, Asn, Val, Pro, Arg, Ala, His, Thr, 716 Trp, or Met; 717 Xaa at position 116 is Lys, Leu, Pro, Thr, Met, Asp, Val, Glu, 718 Arg, Trp, Ser, Asn, His, Ala, Tyr, Phe, Gln, or Ile; 719 Xaa at position 117 is Thr, Ser, Asn, Ile, Trp, Lys, or Pro; 720 Xaa at position 118 is Leu, Ser, Pro, Ala, Glu, Cys, Asp, or 721 722 Xaa at position 119 is Glu, Ser, Lys, Pro, Leu, Thr, Tyr, or 723 Arq; 724 Xaa at position 120 is Asn, Ala, Pro, Leu, His, Val, or Gln;

Xaa at position 121 is Ala, Ser, Ile, Asn, Pro, Lys, Asp, or

```
727
     Xaa at position 122 is Gln, Ser, Met, Trp, Arg, Phe, Pro, His,
728
           Ile, Tyr, or Cys;
729
     Xaa at position 123 is Ala, Met, Glu, His, Ser, Pro, Tyr, or
730
     Leu,
731
732
     wherein from 1 to 14 amino acids can optionally be deleted
733
     from the N-terminus and/or from 1 to 15 amino acids can
734
     optionally be deleted from the C-terminus of said modified
735
     human IL-3 amino acid sequence; and wherein from 1 to 44 of
736
     the amino acids designated by Xaa are different from the
737
     corresponding amino acids of native (1-133) human interleukin-
738
     3; and
739
740
741
           (V) a colony stimulating factor:
742
743
     and wherein L<sub>1</sub> is a linker capable of linking R<sub>1</sub> to R<sub>2</sub>;
744
745
           with the proviso that at least R1 or R2 is selected from
746
     the polypeptide of formula (I), (II), or (III); and
747
748
           said hematopoietic protein can optionally be immediately
     preceded by (methionine^{-1}), (alanine^{-1}) or (methionine^{-2}, alanine^{-1}
749
     1).
750
 1
               A hematopoietic protein comprising; an amino acid sequence
 2
     of the formula:
 3
 4
                R_1-L_1-R_2, R_2-L_1-R_1, R_1-R_2, or R_2-R_1
 5
 6
          wherein R<sub>1</sub> and R<sub>2</sub> are independently selected from the
 7
     group consisting of:
 8
 9
           (I) A polypeptide comprising; a modified human G-CSF
10
     amino acid sequence of the formula:
```

```
12
    1
                                          10
13
    Xaa Xaa Xaa Gly Pro Ala Ser Ser Leu Pro Gln Ser Xaa
14
15
                             20
16
    Leu Leu Xaa Xaa Glu Gln Val Xaa Lys Xaa Gln Gly Xaa Gly
17
18
        30
                                                  40
19
    Ala Xaa Leu Gln Glu Xaa Leu Xaa Ala Thr Tyr Lys Leu Xaa Xaa
20
21
                             50
22
    Xaa Glu Xaa Xaa Val Xaa Xaa Gly His Ser Xaa Gly Ile Pro Trp
23
24
25
    Ala Pro Leu Ser Ser Xaa Pro Ser Xaa Ala Leu Xaa Leu Ala Gly
26
27
                             80
28
    Xaa Leu Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu
29
30
        90
                                                  100
31
    Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu
32
33
                             110
34
    Xaa Thr Leu Gln Xaa Asp Val Ala Asp Phe Ala Xaa Thr Ile Trp
35
36
        120
                                                  130
37
    Gln Gln Met Glu Xaa Xaa Gly Met Ala Pro Ala Leu Gln Pro Thr
38
39
40
    Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Xaa Gln Xaa Xaa Ala
41
42
        150
    Gly Gly Val Leu Val Ala Ser Xaa Leu Gln Xaa Phe Leu Xaa Xaa
43
44
45
                             170
46
    Ser Tyr Arg Val Leu Xaa Xaa Leu Ala Gln Pro (SEO ID NO:1)
47
48
    wherein
49
50
    Xaa at position 1 is Thr, Ser, Arg, Tyr or Gly;
51
    Xaa at position 2 is Pro or Leu;
52
    Xaa at position 3 is Leu, Arg, Tyr or Ser;
53
    Xaa at position 13 is Phe, Ser, His, Thr or Pro;
54
    Xaa at position 16 is Lys, Pro, Ser, Thr or His;
    Xaa at position 17 is Cys, Ser, Gly, Ala, Ile, Tyr or
55
56
    Xaa at position 18 is Leu, Thr, Pro, His, Ile or Cys;
57
    Xaa at position 22 is Arg, Tyr, Ser, Thr or Ala;
58
    Xaa at position 24 is Ile, Pro, Tyr or Leu;
```

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59
    Xaa at position 27 is Asp, or Gly;
60
    Xaa at position 30 is Ala, Ile, Leu or Gly;
61
    Xaa at position 34 is Lys or Ser;
62
    Xaa at position 36 is Cys or Ser;
63
    Xaa at position 42 is Cys or Ser;
64
    Xaa at position 43 is His, Thr, Gly, Val, Lys, Trp, Ala,
65
          Arg, Cys, or Leu;
66
    Xaa at position 44 is Pro, Gly, Arg, Asp, Val, Ala, His,
67
          Trp, Gln, or Thr;
68
    Xaa at position 46 is Glu, Arq, Phe, Arq, Ile or Ala;
69
    Xaa at position 47 is Leu or Thr;
70
    Xaa at position 49 is Leu, Phe, Arg or Ser;
71
    Xaa at position 50 is Leu, Ile, His, Pro or Tyr;
72
    Xaa at position 54 is Leu or His;
73
    Xaa at position 64 is Cys or Ser;
    Xaa at position 67 is Gln, Lys, Leu or Cys;
74
    Xaa at position 70 is Gln, Pro, Leu, Arg or Ser;
75
    Xaa at position 74 is Cys or Ser;
76
77
    Xaa at position 104 is Asp, Gly or Val;
78
    Xaa at position 108 is Leu, Ala, Val, Arg, Trp, Gln or
79
          Gly;
80
    Xaa at position 115 is Thr, His, Leu or Ala;
81
    Xaa at position 120 is Gln, Gly, Arg, Lys or His
    Xaa at position 123 is Glu, Arg, Phe or Thr
82
83
    Xaa at position 144 is Phe, His, Arg, Pro, Leu, Gln or
84
          Glu;
85
    Xaa at position 146 is Arg or Gln;
86
    Xaa at position 147 is Arg or Gln;
87
    Xaa at position 156 is His, Gly or Ser;
88
    Xaa at position 159 is Ser, Arg, Thr, Tyr, Val or Gly;
    Xaa at position 162 is Glu, Leu, Gly or Trp;
89
90
    Xaa at position 163 is Val, Gly, Arg or Ala;
91
    Xaa at position 169 is Arg, Ser, Leu, Arg or Cys;
92
    Xaa at position 170 is His, Arg or Ser,
93
94
     wherein optionally 1-11 amino acids from the N-terminus and 1-
95
     5 from the C-terminus can optionally be deleted from said
96
    modified human G-CSF amino acid sequence; and
97
98
     wherein the N-terminus is joined to the C-terminus directly or
99
     through a linker capable of joining the N-terminus to the C-
100
     terminus and having new C- and N-termini at amino acids;
101
102
103
     38-39
                            62-63
                                               123-124
104
    39-40
                            63-64
                                               124-125
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105
    40 - 41
                       64-65
                                        125-126
106
    41-42
                       65-66
                                        126-127
107
    42-43
                       66-67
                                        128-129
                                        128-129
108
    43 - 44
                       67-68
109
    45 - 46
                       68-69
                                        129-130
110
    48 - 49
                       69-70
                                        130-131
111
    49-50
                       70-71
                                        131-132
112
    52-53
                       71-72
                                        132-133
                       91-92
113
    53-54
                                        133-134
114
    54-55
                       92-93
                                        134-135
115
    55-56
                       93 - 94
                                        135-136
116
    56-57
                       94 - 95
                                        136-137
117
    57-58
                       95 - 96
                                        137-138
118
    58 - 59
                       96 - 97
                                        138-139
119
    59-60
                       97-98
                                        139-140
120
    60-61
                       98-99
                                        140-141
121
    61 - 62
                       99-100
                                        141-142
122
                                        or 142-143
123
                                        respectively;
124
125
        (II) A polypeptide comprising; a modified human IL-3
126
    amino acid sequence of the formula:
127
128
    Ala Pro Met Thr Gln Thr Thr Ser Leu Lys Thr Ser Trp Val Asn
129
                  5
                                   10
                                                    15
130
131
    132
                  20
                                   25
                                                     30
133
134
    Xaa Xaa Xaa Xaa Xaa Xaa Xaa Asn Xaa Xaa Xaa Xaa Xaa
135
                  35
                                   40
                                                     45
136
137
    138
                  50
                                   55
                                                     60
139
140
    141
                                   70
                                                    75
                  65
142
143
    144
                  80
                                                     90
                                   85
```

```
145
146
    147
                    95
                                       100
                                                          105
148
149
    150
                    110
                                       115
                                                          120
151
152
    Xaa Xaa Xaa Gln Gln Thr Thr Leu Ser Leu Ala Ile Phe
153
                    125
                                       130
                                            (SEQ ID NO:2)
154
155
    wherein Xaa at position 17 is Ser, Lys, Gly, Asp, Met, Gln, or
156
157
    Xaa at position 18 is Asn, His, Leu, Ile, Phe, Arg, or Gln;
158
    Xaa at position 19 is Met, Phe, Ile, Arg, Gly, Ala, or Cys;
159
    Xaa at position 20 is Ile, Cys, Gln, Glu, Arg, Pro, or Ala;
160
    Xaa at position 21 is Asp, Phe, Lys, Arg, Ala, Gly, Glu, Gln,
161
    Asn,
         Thr, Ser or Val;
162
163
    Xaa at position 22 is Glu, Trp, Pro, Ser, Ala, His, Asp, Asn,
164
    Gln,
165
         Leu, Val or Gly;
166
    Xaa at position 23 is Ile, Val, Ala, Gly, Trp, Lys, Phe,
167
         Leu, Ser, or Arg;
168
    Xaa at position 24 is Ile, Gly, Val, Arg, Ser, Phe, or Leu;
    Xaa at position 25 is Thr, His, Gly, Gln, Arg, Pro, or Ala;
169
170
    Xaa at position 26 is His, Thr, Phe, Gly, Arg, Ala, or Trp;
171
    Xaa at position 27 is Leu, Gly, Arg, Thr, Ser, or Ala;
172
    Xaa at position 28 is Lys, Arg, Leu, Gln, Gly, Pro, Val or
173
    Trp;
174
    Xaa at position 29 is Gln, Asn, Leu, Pro, Arg, or Val;
175
    Xaa at position 30 is Pro, His, Thr, Gly, Asp, Gln, Ser, Leu,
176
    or
         Lys;
177
    Xaa at position 31 is Pro, Asp, Gly, Ala, Arg, Leu, or Gln;
178
    Xaa at position 32 is Leu, Val, Arg, Gln, Asn, Gly, Ala, or
179
    Glu;
180
    Xaa at position 33 is Pro, Leu, Gln, Ala, Thr, or Glu;
```

Xaa at position 34 is Leu, Val, Gly, Ser, Lys, Glu, Gln, Thr, 181 182 Arg, Ala, Phe, Ile or Met; 183 Xaa at position 35 is Leu, Ala, Gly, Asn, Pro, Gln, or Val; 184 Xaa at position 36 is Asp, Leu, or Val; 185 Xaa at position 37 is Phe, Ser, Pro, Trp, or Ile; 186 Xaa at position 38 is Asn, or Ala; Xaa at position 40 is Leu, Trp, or Arg; 187 188 Xaa at position 41 is Asn, Cys, Arg, Leu, His, Met, or Pro; Xaa at position 42 is Gly, Asp, Ser, Cys, Asn, Lys, Thr, Leu, 189 190 Val, Glu, Phe, Tyr, Ile, Met or Ala; 191 Xaa at position 43 is Glu, Asn, Tyr, Leu, Phe, Asp, Ala, Cys, 192 Gln, Arg, Thr, Gly or Ser; 193 Xaa at position 44 is Asp, Ser, Leu, Arg, Lys, Thr, Met, Trp, 194 Glu, Asn, Gln, Ala or Pro; 195 Xaa at position 45 is Gln, Pro, Phe, Val, Met, Leu, Thr, Lys, 196 Trp, Asp, Asn, Arg, Ser, Ala, Ile, Glu or His; 197 Xaa at position 46 is Asp, Phe, Ser, Thr, Cys, Glu, Asn, Gln, 198 Lys, His, Ala, Tyr, Ile, Val or Gly; 199 Xaa at position 47 is Ile, Gly, Val, Ser, Arg, Pro, or His; 200 Xaa at position 48 is Leu, Ser, Cys, Arg, Ile, His, Phe, Glu, 201 Lys, Thr, Ala, Met, Val or Asn; 202 Xaa at position 49 is Met, Arg, Ala, Gly, Pro, Asn, His, or 203 Asp; 204 Xaa at position 50 is Glu, Leu, Thr, Asp, Tyr, Lys, Asn, Ser, 205 Ala, Ile, Val, His, Phe, Met or Gln; 206 Xaa at position 51 is Asn, Arg, Met, Pro, Ser, Thr, or His; 207 Xaa at position 52 is Asn, His, Arg, Leu, Gly, Ser, or Thr; 208 Xaa at position 53 is Leu, Thr, Ala, Gly, Glu, Pro, Lys, Ser, 209 or Met; 210 Xaa at position 54 is Arg, Asp, Ile, Ser, Val, Thr, Gln, Asn, 211 Lys, His, Ala or Leu; 212 Xaa at position 55 is Arg, Thr, Val, Ser, Leu, or Gly; 213 Xaa at position 56 is Pro, Gly, Cys, Ser, Gln, Glu, Arg, His, 214 Thr, Ala, Tyr, Phe, Leu, Val or Lys; 215 Xaa at position 57 is Asn or Gly;

Xaa at position 58 is Leu, Ser, Asp, Arg, Gln, Val, or Cys;

- 217 Xaa at position 59 is Glu Tyr, His, Leu, Pro, or Arg;
- 218 Xaa at position 60 is Ala, Ser, Pro, Tyr, Asn, or Thr;
- 219 Xaa at position 61 is Phe, Asn, Glu, Pro, Lys, Arg, or Ser;
- 220 Xaa at position 62 is Asn, His, Val, Arg, Pro, Thr, Asp, or
- 221 Ile;
- 222 Xaa at position 63 is Arg, Tyr, Trp, Lys, Ser, His, Pro, or
- 223 Val;
- 224 Xaa at position 64 is Ala, Asn, Pro, Ser, or Lys;
- 225 Xaa at position 65 is Val, Thr, Pro, His, Leu, Phe, or Ser;
- 226 Xaa at position 66 is Lys, Ile, Arg, Val, Asn, Glu, or Ser;
- 227 Xaa at position 67 is Ser, Ala, Phe, Val, Gly, Asn, Ile, Pro,
- 228 or His;
- 229 Xaa at position 68 is Leu, Val, Trp, Ser, Ile, Phe, Thr, or
- 230 His;
- 231 Xaa at position 69 is Gln, Ala, Pro, Thr, Glu, Arg, Trp, Gly,
- 232 or Leu;
- 233 Xaa at position 70 is Asn, Leu, Val, Trp, Pro, or Ala;
- 234 Xaa at position 71 is Ala, Met, Leu, Pro, Arg, Glu, Thr, Gln,
- 235 Trp, or Asn;
- 236 Xaa at position 72 is Ser, Glu, Met, Ala, His, Asn, Arg, or
- 237 Asp;
- 238 Xaa at position 73 is Ala, Glu, Asp, Leu, Ser, Gly, Thr, or
- 239 Arg;
- 240 Xaa at position 74 is Ile, Met, Thr, Pro, Arg, Gly, Ala;
- 241 Xaa at position 75 is Glu, Lys, Gly, Asp, Pro, Trp, Arg, Ser,
- 242 Gln, or Leu;
- 243 Xaa at position 76 is Ser, Val, Ala, Asn, Trp, Glu, Pro, Gly,
- 244 or Asp;
- 245 Xaa at position 77 is Ile, Ser, Arg, Thr, or Leu;
- 246 Xaa at position 78 is Leu, Ala, Ser, Glu, Phe, Gly, or Arg;
- 247 Xaa at position 79 is Lys, Thr, Asn, Met, Arg, Ile, Gly, or
- 248 Asp;
- 249 Xaa at position 80 is Asn, Trp, Val, Gly, Thr, Leu, Glu, or
- 250 Arg;
- 251 Xaa at position 81 is Leu, Gln, Gly, Ala, Trp, Arg, Val, or
- 252 Lys;

Xaa at position 82 is Leu, Gln, Lys, Trp, Arg, Asp, Glu, Asn, 253 254 His, Thr, Ser, Ala, Tyr, Phe, Ile, Met or Val; 255 Xaa at position 83 is Pro, Ala, Thr, Trp, Arg, or Met; 256 Xaa at position 84 is Cys, Glu, Gly, Arg, Met, or Val; 257 Xaa at position 85 is Leu, Asn, Val, or Gln; 258 Xaa at position 86 is Pro, Cys, Arg, Ala, or Lys; Xaa at position 87 is Leu, Ser, Trp, or Gly; 259 260 Xaa at position 88 is Ala, Lys, Arg, Val, or Trp; 261 Xaa at position 89 is Thr, Asp, Cys, Leu, Val, Glu, His, Asn, 262 or Ser; 263 Xaa at position 90 is Ala, Pro, Ser, Thr, Gly, Asp, Ile, or 264 265 Xaa at position 91 is Ala, Pro, Ser, Thr, Phe, Leu, Asp, or 266 His; 267 Xaa at position 92 is Pro, Phe, Arg, Ser, Lys, His, Ala, Gly, 268 Ile Leu; 269 Xaa at position 93 is Thr, Asp, Ser, Asn, Pro, Ala, Leu, or 270 Arq; 271 Xaa at position 94 is Arg, Ile, Ser, Glu, Leu, Val, Gln, Lys, 272 His, Ala, or Pro; 273 Xaa at position 95 is His, Gln, Pro, Arg, Val, Leu, Gly, Thr, 274 Asn, Lys, Ser, Ala, Trp, Phe, Ile, or Tyr; 275 Xaa at position 96 is Pro, Lys, Tyr, Gly, Ile, or Thr; 276 Xaa at position 97 is Ile, Val, Lys, Ala, or Asn; 277 Xaa at position 98 is His, Ile, Asn, Leu, Asp, Ala, Thr, 278 Glu, Gln, Ser, Phe, Met, Val, Lys, Arg, Tyr or Pro; 279 Xaa at position 99 is Ile, Leu, Arg, Asp, Val, Pro, Gln, 280 Gly, Ser, Phe, or His; 281 Xaa at position 100 is Lys, Tyr, Leu, His, Arq, Ile, Ser, Gln, 282 or Pro; 283 Xaa at position 101 is Asp, Pro, Met, Lys, His, Thr, Val, 284 Tyr, Glu, Asn, Ser, Ala, Gly, Ile, Leu, or Gln; 285 Xaa at position 102 is Gly, Leu, Glu, Lys, Ser, Tyr, or Pro; 286 Xaa at position 103 is Asp, or Ser;

Gln, Lys, Ala, Phe, or Gly;

Xaa at position 104 is Trp, Val, Cys, Tyr, Thr, Met, Pro, Leu,

287

- 289 Xaa at position 105 is Asn, Pro, Ala, Phe, Ser, Trp, Gln, Tyr, 290 Leu, Lys, Ile, Asp, or His; 291 Xaa at position 106 is Glu, Ser, Ala, Lys, Thr, Ile, Gly, or 292 Pro; 293 Xaa at position 108 is Arg, Lys, Asp, Leu, Thr, Ile, Gln, His, 294 Ser, Ala or Pro; 295 Xaa at position 109 is Arg, Thr, Pro, Glu, Tyr, Leu, Ser, or 296 Gly; 297 Xaa at position 110 is Lys, Ala, Asn, Thr, Leu, Arg, Gln, His, 298 Glu, Ser, or Trp; 299 Xaa at position 111 is Leu, Ile, Arg, Asp, or Met; 300 Xaa at position 112 is Thr, Val, Gln, Tyr, Glu, His, Ser, or 301 Phe: 302 Xaa at position 113 is Phe, Ser, Cys, His, Gly, Trp, Tyr, Asp, 303 Lys, Leu, Ile, Val or Asn; 304 Xaa at position 114 is Tyr, Cys, His, Ser, Trp, Arg, or Leu; 305 Xaa at position 115 is Leu, Asn, Val, Pro, Arg, Ala, His, Thr, 306 Trp, or Met; 307 Xaa at position 116 is Lys, Leu, Pro, Thr, Met, Asp, Val, Glu, 308 Arg, Trp, Ser, Asn, His, Ala, Tyr, Phe, Gln, or Ile; 309 Xaa at position 117 is Thr, Ser, Asn, Ile, Trp, Lys, or Pro; 310 Xaa at position 118 is Leu, Ser, Pro, Ala, Glu, Cys, Asp, or 311 Tyr; 312 Xaa at position 119 is Glu, Ser, Lys, Pro, Leu, Thr, Tyr, or 313 Arg; 314 Xaa at position 120 is Asn, Ala, Pro, Leu, His, Val, or Gln; 315 Xaa at position 121 is Ala, Ser, Ile, Asn, Pro, Lys, Asp, or 316 Gly; 317 Xaa at position 122 is Gln, Ser, Met, Trp, Arg, Phe, Pro, His, 318 Ile, Tyr, or Cys; 319 Xaa at position 123 is Ala, Met, Glu, His, Ser, Pro, Tyr, or 320 Leu, 321
- 322 wherein from 1 to 14 amino acids can optionally be deleted
- 323 from the N-terminus and/or from 1 to 15 amino acids can
- 324 optionally be deleted from the C-terminus of said modified

human IL-3 amino acid sequence; wherein from 0 to 44 of the amino acids designated by Xaa are different from the corresponding amino acids of native (1-133) human interleukin-328 3; and

329 330

331

wherein the N-terminus is joined to the C-terminus directly or through a linker ( $L_2$ ), capable of joining the N-terminus to

332 the C-terminus and having new C- and N-termini at amino acids:

333

		1
26-27	49-50	83-84
27-28	50-51	84-85
28-29	51-52	85-86
29-30	52-53	86-87
30-31	53-54	87-88
31-32	54-55	88-89
32-33	64-65	89-90
33-34	65-66	90-91
34-35	66-67	91-92
35-36	67-68	92-93
36-37	68-69	97-98
37-38	69-70	98-99
38-39	70-71	99-100
39-40	71-72	100-101
40-41	72-73	101-102
41-42	82-83	102-103
		or 103-104
		respectively;

334335

336

(III) A polypeptide comprising; a modified human c-mpl ligand amino acid sequence of the formula:

337338339

SerProAlaProProAlaCysAspLeuArgValLeuSerLysLeuLeuArgAspSer 1 5 10 15

340341342

HisValLeuHisSerArgLeuSerGlnCysProGluValHisProLeuProThrPro 20 25 30 35

343344345

ValLeuLeuProAlaValAspPheSerLeuGlyGluTrpLysThrGlnMetGluGlu 40 45 50 55

346347348

349

ThrLysAlaGlnAspIleLeuGlyAlaValThrLeuLeuLeuGluGlyValMetAla 60 65 70 75

```
350
351
     AlaArgGlyGlnLeuGlyProThrCysLeuSerSerLeuLeuGlyGlnLeuSerGly
352
                              85
                                              90
353
354
     GlnValArgLeuLeuGlyAlaLeuGlnSerLeuLeuGlyThrGlnXaaXaaXaa
355
                                 105
356
357
     XaaGlyArgThrThrAlaHisLysAspProAsnAlaIlePheLeuSerPheGlnHis
358
     115
                    120
                                    125
359
360
     LeuLeuArgGlyLysValArgPheLeuMetLeuValGlyGlySerThrLeuCysVal
361
        135
                        140
                                       145
                                                       150
362
363
     Arg (SEQ ID NO:256)
364
     153
365
366
     wherein
367
368
     Xaa at position 112 is deleted or Leu, Ala, Val, Ile,
369
          Pro, Phe, Trp, or Met;
370
     Xaa at position 113 is deleted or Pro, Phe, Ala, Val,
                                                              Leu,
371
     Ile, Trp, or Met;
372
     Xaa at position 114 is deleted or Pro, Phe, Ala, Val, Leu,
373
     Ile, Trp, or Met;
374
     Xaa at position 115 is deleted or Gln, Gly, Ser, Thr,
                                                              Tyr, or
375
     Asn,
376
377
     wherein the N-terminus is joined to the C-terminus directly or
378
     through a linker (L2) capable of joining the N-terminus to the
     C-terminus and having new C- and N-termini at amino acids:
379
380
```

26-27	51-52	108-109
27-28	52-53	109-110
28-29	53-54	110-111
29-30	54-55	111-112
30-31	55-56	112-113
32-33	56-57	113-114
33-34	57-58	114-115
34-35	58-59	115-116
36-37	59-60	116-117
37-38	78-79	117-118

38-39	79-80	118-119
40-41	80-81	119-120
41-42	81-82	120-121
42-43	82-83	121-122
43-44	83-84	122-123
44-45	84-85	123-124
46-47	85-86	124-125
47-48	86-87	125-126
48-49	87-88	126-127
50-51	88-89	or 127-128
		respectively;

(IV) A polypeptide comprising; a modified human IL-3 amino acid sequence of the formula:

387 Ala Pro Met Thr Gln Thr Thr Ser Leu Lys Thr Ser Trp Val Asn 388 1 5 10 15

```
408
     409
                     110
                                         115
                                                             120
410
411
     Xaa Xaa Xaa Gln Gln Thr Thr Leu Ser Leu Ala Ile Phe
412
                     125
                                         130 (SEQ ID NO:2)
413
414
     wherein Xaa at position 17 is Ser, Lys, Gly, Asp, Met, Gln, or
415
     Arg;
416
     Xaa at position 18 is Asn, His, Leu, Ile, Phe, Arg, or Gln;
417
     Xaa at position 19 is Met, Phe, Ile, Arg, Gly, Ala, or Cys;
418
     Xaa at position 20 is Ile, Cys, Gln, Glu, Arg, Pro, or Ala;
419
     Xaa at position 21 is Asp, Phe, Lys, Arg, Ala, Gly, Glu, Gln,
420
     Asn,
421
          Thr, Ser or Val;
422
     Xaa at position 22 is Glu, Trp, Pro, Ser, Ala, His, Asp, Asn,
423
     Gln,
424
          Leu, Val or Gly;
425
     Xaa at position 23 is Ile, Val, Ala, Gly, Trp, Lys, Phe,
426
          Leu, Ser, or Arg;
     Xaa at position 24 is Ile, Gly, Val, Arg, Ser, Phe, or Leu;
427
428
     Xaa at position 25 is Thr, His, Gly, Gln, Arg, Pro, or Ala;
429
     Xaa at position 26 is His, Thr, Phe, Gly, Arg, Ala, or Trp;
430
     Xaa at position 27 is Leu, Gly, Arg, Thr, Ser, or Ala;
431
     Xaa at position 28 is Lys, Arg, Leu, Gln, Gly, Pro, Val or
432
     Trp;
433
     Xaa at position 29 is Gln, Asn, Leu, Pro, Arg, or Val;
434
     Xaa at position 30 is Pro, His, Thr, Gly, Asp, Gln, Ser, Leu,
435
     or Lys;
436
     Xaa at position 31 is Pro, Asp, Gly, Ala, Arg, Leu, or Gln;
437
     Xaa at position 32 is Leu, Val, Arg, Gln, Asn, Gly, Ala, or
438
     Glu;
439
     Xaa at position 33 is Pro, Leu, Gln, Ala, Thr, or Glu;
440
     Xaa at position 34 is Leu, Val, Gly, Ser, Lys, Glu, Gln, Thr,
441
          Arg, Ala, Phe, Ile or Met;
442
     Xaa at position 35 is Leu, Ala, Gly, Asn, Pro, Gln, or Val;
443
     Xaa at position 36 is Asp, Leu, or Val;
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444 Xaa at position 37 is Phe, Ser, Pro, Trp, or Ile; 445 Xaa at position 38 is Asn, or Ala; 446 Xaa at position 40 is Leu, Trp, or Arg; 447 Xaa at position 41 is Asn, Cys, Arg, Leu, His, Met, or Pro; 448 Xaa at position 42 is Gly, Asp, Ser, Cys, Asn, Lys, Thr, Leu, 449 Val, Glu, Phe, Tyr, Ile, Met or Ala; 450 Xaa at position 43 is Glu, Asn, Tyr, Leu, Phe, Asp, Ala, Cys, 451 Gln, Arg, Thr, Gly or Ser; 452 Xaa at position 44 is Asp, Ser, Leu, Arg, Lys, Thr, Met, Trp, 453 Glu, Asn, Gln, Ala or Pro; 454 Xaa at position 45 is Gln, Pro, Phe, Val, Met, Leu, Thr, Lys, 455 Trp, Asp, Asn, Arg, Ser, Ala, Ile, Glu or His; 456 Xaa at position 46 is Asp, Phe, Ser, Thr, Cys, Glu, Asn, Gln, 457 Lys, His, Ala, Tyr, Ile, Val or Gly; 458 Xaa at position 47 is Ile, Gly, Val, Ser, Arg, Pro, or His; 459 Xaa at position 48 is Leu, Ser, Cys, Arg, Ile, His, Phe, Glu, 460 Lys, Thr, Ala, Met, Val or Asn; 461 Xaa at position 49 is Met, Arg, Ala, Gly, Pro, Asn, His, or 462 Asp; 463 Xaa at position 50 is Glu, Leu, Thr, Asp, Tyr, Lys, Asn, Ser, 464 Ala, Ile, Val, His, Phe, Met or Gln; 465 Xaa at position 51 is Asn, Arg, Met, Pro, Ser, Thr, or His; 466 Xaa at position 52 is Asn, His, Arg, Leu, Gly, Ser, or Thr; 467 Xaa at position 53 is Leu, Thr, Ala, Gly, Glu, Pro, Lys, Ser, 468 or Met; 469 Xaa at position 54 is Arg, Asp, Ile, Ser, Val, Thr, Gln, Asn, 470 Lys, His, Ala or Leu; 471 Xaa at position 55 is Arg, Thr, Val, Ser, Leu, or Gly; Xaa at position 56 is Pro, Gly, Cys, Ser, Gln, Glu, Arg, His, 472 473 Thr, Ala, Tyr, Phe, Leu, Val or Lys; 474 Xaa at position 57 is Asn or Gly; 475 Xaa at position 58 is Leu, Ser, Asp, Arg, Gln, Val, or Cys; Xaa at position 59 is Glu Tyr, His, Leu, Pro, or Arg; 476 Xaa at position 60 is Ala, Ser, Pro, Tyr, Asn, or Thr; 477

Xaa at position 61 is Phe, Asn, Glu, Pro, Lys, Arg, or Ser;

479 Xaa at position 62 is Asn, His, Val, Arg, Pro, Thr, Asp, or 480 Ile; 481 Xaa at position 63 is Arg, Tyr, Trp, Lys, Ser, His, Pro, or 482 Val; 483 Xaa at position 64 is Ala, Asn, Pro, Ser, or Lys; 484 Xaa at position 65 is Val, Thr, Pro, His, Leu, Phe, or Ser; 485 Xaa at position 66 is Lys, Ile, Arg, Val, Asn, Glu, or Ser; 486 Xaa at position 67 is Ser, Ala, Phe, Val, Gly, Asn, Ile, Pro, 487 or His; 488 Xaa at position 68 is Leu, Val, Trp, Ser, Ile, Phe, Thr, or 489 490 Xaa at position 69 is Gln, Ala, Pro, Thr, Glu, Arg, Trp, Gly, 491 or Leu; Xaa at position 70 is Asn, Leu, Val, Trp, Pro, or Ala; 492 493 Xaa at position 71 is Ala, Met, Leu, Pro, Arg, Glu, Thr, Gln, 494 Trp, or Asn; 495 Xaa at position 72 is Ser, Glu, Met, Ala, His, Asn, Arg, or 496 Asp; 497 Xaa at position 73 is Ala, Glu, Asp, Leu, Ser, Gly, Thr, or 498 Arq; 499 Xaa at position 74 is Ile, Met, Thr, Pro, Arg, Gly, Ala; Xaa at position 75 is Glu, Lys, Gly, Asp, Pro, Trp, Arg, Ser, 500 501 Gln, or Leu; 502 Xaa at position 76 is Ser, Val, Ala, Asn, Trp, Glu, Pro, Gly, 503 or Asp; 504 Xaa at position 77 is Ile, Ser, Arg, Thr, or Leu; 505 Xaa at position 78 is Leu, Ala, Ser, Glu, Phe, Gly, or Arg; 506 Xaa at position 79 is Lys, Thr, Asn, Met, Arg, Ile, Gly, or 507 Asp; 508 Xaa at position 80 is Asn, Trp, Val, Gly, Thr, Leu, Glu, or 509 510 Xaa at position 81 is Leu, Gln, Gly, Ala, Trp, Arg, Val, or 511 Lys; 512 Xaa at position 82 is Leu, Gln, Lys, Trp, Arg, Asp, Glu, Asn,

His, Thr, Ser, Ala, Tyr, Phe, Ile, Met or Val;

Xaa at position 83 is Pro, Ala, Thr, Trp, Arg, or Met;

513

548

549

515 Xaa at position 84 is Cys, Glu, Gly, Arg, Met, or Val; 516 Xaa at position 85 is Leu, Asn, Val, or Gln; 517 Xaa at position 86 is Pro, Cys, Arg, Ala, or Lys; Xaa at position 87 is Leu, Ser, Trp, or Gly; 518 519 Xaa at position 88 is Ala, Lys, Arg, Val, or Trp; 520 Xaa at position 89 is Thr, Asp, Cys, Leu, Val, Glu, His, Asn, 521 or 522 Xaa at position 90 is Ala, Pro, Ser, Thr, Gly, Asp, Ile, or 523 Met; 524 Xaa at position 91 is Ala, Pro, Ser, Thr, Phe, Leu, Asp, or 525 526 Xaa at position 92 is Pro, Phe, Arg, Ser, Lys, His, Ala, Gly, 527 Ile or Leu; 528 Xaa at position 93 is Thr, Asp, Ser, Asn, Pro, Ala, Leu, or 529 Ara; 530 Xaa at position 94 is Arg, Ile, Ser, Glu, Leu, Val, Gln, Lys, 531 His, Ala, or Pro; 532 Xaa at position 95 is His, Gln, Pro, Arg, Val, Leu, Gly, Thr, 533 Asn, Lys, Ser, Ala, Trp, Phe, Ile, or Tyr; 534 Xaa at position 96 is Pro, Lys, Tyr, Gly, Ile, or Thr; 535 Xaa at position 97 is Ile, Val, Lys, Ala, or Asn; 536 Xaa at position 98 is His, Ile, Asn, Leu, Asp, Ala, Thr, 537 Glu, Gln, Ser, Phe, Met, Val, Lys, Arg, Tyr or Pro; 538 Xaa at position 99 is Ile, Leu, Arg, Asp, Val, Pro, Gln, 539 Gly, Ser, Phe, or His; 540 Xaa at position 100 is Lys, Tyr, Leu, His, Arg, Ile, Ser, Gln, 541 or Pro; 542 Xaa at position 101 is Asp, Pro, Met, Lys, His, Thr, Val, 543 Tyr, Glu, Asn, Ser, Ala, Gly, Ile, Leu, or Gln; 544 Xaa at position 102 is Gly, Leu, Glu, Lys, Ser, Tyr, or Pro; 545 Xaa at position 103 is Asp, or Ser; 546 Xaa at position 104 is Trp, Val, Cys, Tyr, Thr, Met, Pro, Leu,

Xaa at position 105 is Asn, Pro, Ala, Phe, Ser, Trp, Gln, Tyr,

Gln, Lys, Ala, Phe, or Gly;

Leu, Lys, Ile, Asp, or His;

584

585

550 Xaa at position 106 is Glu, Ser, Ala, Lys, Thr, Ile, Gly, or 551 Pro; 552 Xaa at position 108 is Arg, Lys, Asp, Leu, Thr, Ile, Gln, His, 553 Ser, Ala or Pro; 554 Xaa at position 109 is Arg, Thr, Pro, Glu, Tyr, Leu, Ser, or 555 Gly; 556 Xaa at position 110 is Lys, Ala, Asn, Thr, Leu, Arg, Gln, His, Glu, Ser, or Trp; 557 558 Xaa at position 111 is Leu, Ile, Arg, Asp, or Met; 559 Xaa at position 112 is Thr, Val, Gln, Tyr, Glu, His, Ser, or 560 Phe; 561 Xaa at position 113 is Phe, Ser, Cys, His, Gly, Trp, Tyr, Asp, 562 Lys, Leu, Ile, Val or Asn; 563 Xaa at position 114 is Tyr, Cys, His, Ser, Trp, Arg, or Leu; 564 Xaa at position 115 is Leu, Asn, Val, Pro, Arg, Ala, His, Thr, 565 Trp, or Met; 566 Xaa at position 116 is Lys, Leu, Pro, Thr, Met, Asp, Val, Glu, 567 Arg, Trp, Ser, Asn, His, Ala, Tyr, Phe, Gln, or Ile; 568 Xaa at position 117 is Thr, Ser, Asn, Ile, Trp, Lys, or Pro; Xaa at position 118 is Leu, Ser, Pro, Ala, Glu, Cys, Asp, or 569 570 571 Xaa at position 119 is Glu, Ser, Lys, Pro, Leu, Thr, Tyr, or 572 Arq; 573 Xaa at position 120 is Asn, Ala, Pro, Leu, His, Val, or Gln; 574 Xaa at position 121 is Ala, Ser, Ile, Asn, Pro, Lys, Asp, or 575 576 Xaa at position 122 is Gln, Ser, Met, Trp, Arg, Phe, Pro, His, 577 Ile, Tyr, or Cys; 578 Xaa at position 123 is Ala, Met, Glu, His, Ser, Pro, Tyr, or 579 Leu; 580 581 wherein from 1 to 14 amino acids can optionally be deleted from the N-terminus and/or from 1 to 15 amino acids can 582

optionally be deleted from the C-terminus of said modified

human IL-3 amino acid sequence; and wherein from 1 to 44 of

the amino acids designated by Xaa are different from the

```
586
     corresponding amino acids of native (1-133) human interleukin-
587
     3; and
588
589
590
           (V) a colony stimulating factor
591
592
     wherein L1 is a linker capable of linking R1 to R2
593
594
          with the proviso that at least R1 or R2 is selected from
595
     the polypeptide of formula (I), (II), or (III) and
596
597
          said hematopoietic protein can optionally be immediately
     preceded by (methionine^{-1}), (alanine^{-1}) or (methionine^{-2}),
598
     alanine^{-1}).
599
 1
               A hematopoietic protein comprising an amino acid sequence
 2
     of the formula:
 3
 4
                R_1-L_1-R_2, R_2-L_1-R_1, R_1-R_2, or R_2-R_1
 5
 6
          wherein R<sub>1</sub> and R<sub>2</sub> are independently selected from the
 7
     group consisting of:
 8
 9
           (I) A polypeptide comprising; a modified human G-CSF
10
     amino acid sequence of the formula:
11
12
13
     Xaa Xaa Xaa Gly Pro Ala Ser Ser Leu Pro Gln Ser Xaa
14
15
                               20
16
     Leu Leu Xaa Xaa Glu Gln Val Xaa Lys Xaa Gln Gly Xaa Gly
17
18
         30
                                                     40
19
     Ala Xaa Leu Gln Glu Xaa Leu Xaa Ala Thr Tyr Lys Leu Xaa Xaa
20
21
                               50
22
     Xaa Glu Xaa Xaa Val Xaa Xaa Gly His Ser Xaa Gly Ile Pro Trp
23
24
         60
                                                     70
25
     Ala Pro Leu Ser Ser Xaa Pro Ser Xaa Ala Leu Xaa Leu Ala Gly
```

```
26
27
                             80
28
    Xaa Leu Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu
29
30
                                                  100
    Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu
31
32
33
                             110
34
    Xaa Thr Leu Gln Xaa Asp Val Ala Asp Phe Ala Xaa Thr Ile Trp
35
36
        120
37
    Gln Gln Met Glu Xaa Xaa Gly Met Ala Pro Ala Leu Gln Pro Thr
38
39
                             140
40
    Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Xaa Gln Xaa Xaa Ala
41
42
        150
                                                  160
43
    Gly Gly Val Leu Val Ala Ser Xaa Leu Gln Xaa Phe Leu Xaa Xaa
44
45
                             170
46
    Ser Tyr Arg Val Leu Xaa Xaa Leu Ala Gln Pro (SEQ ID NO:1)
47
48
    wherein
49
50
    Xaa at position 1 is Thr, Ser, Arg, Tyr or Gly;
51
    Xaa at position 2 is Pro or Leu;
52
    Xaa at position 3 is Leu, Arg, Tyr or Ser;
53
    Xaa at position 13 is Phe, Ser, His, Thr or Pro;
    Xaa at position 16 is Lys, Pro, Ser, Thr or His;
54
55
    Xaa at position 17 is Cys, Ser, Gly, Ala, Ile, Tyr or
56
         Arq;
57
    Xaa at position 18 is Leu, Thr, Pro, His, Ile or Cys;
    Xaa at position 22 is Arg, Tyr, Ser, Thr or Ala;
58
59
    Xaa at position 24 is Ile, Pro, Tyr or Leu;
60
    Xaa at position 27 is Asp, or Gly;
61
    Xaa at position 30 is Ala, Ile, Leu or Gly;
62
    Xaa at position 34 is Lys or Ser;
63
    Xaa at position 36 is Cys or Ser;
64
    Xaa at position 42 is Cys or Ser;
65
    Xaa at position 43 is His, Thr, Gly, Val, Lys, Trp, Ala,
66
         Arg, Cys, or Leu;
67
    Xaa at position 44 is Pro, Gly, Arg, Asp, Val, Ala, His,
68
         Trp, Gln, or Thr;
69
    Xaa at position 46 is Glu, Arg, Phe, Arg, Ile or Ala;
70
    Xaa at position 47 is Leu or Thr;
    Xaa at position 49 is Leu, Phe, Arg or Ser;
71
72
    Xaa at position 50 is Leu, Ile, His, Pro or Tyr;
```

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73
     Xaa at position 54 is Leu or His;
74
     Xaa at position 64 is Cys or Ser;
75
     Xaa at position 67 is Gln, Lys, Leu or Cys;
76
     Xaa at position 70 is Gln, Pro, Leu, Arg or Ser;
77
     Xaa at position 74 is Cys or Ser;
78
     Xaa at position 104 is Asp, Gly or Val;
79
     Xaa at position 108 is Leu, Ala, Val, Arg, Trp, Gln or
80
          Gly;
81
     Xaa at position 115 is Thr, His, Leu or Ala;
82
     Xaa at position 120 is Gln, Gly, Arg, Lys or His
83
     Xaa at position 123 is Glu, Arg, Phe or Thr
     Xaa at position 144 is Phe, His, Arg, Pro, Leu, Gln or
84
85
          Glu:
86
     Xaa at position 146 is Arg or Gln;
87
     Xaa at position 147 is Arg or Gln;
88
     Xaa at position 156 is His, Gly or Ser;
89
     Xaa at position 159 is Ser, Arg, Thr, Tyr, Val or Gly;
90
     Xaa at position 162 is Glu, Leu, Gly or Trp;
91
     Xaa at position 163 is Val, Gly, Arg or Ala;
92
     Xaa at position 169 is Arg, Ser, Leu, Arg or Cys;
93
     Xaa at position 170 is His, Arg or Ser,
94
95
     wherein optionally 1-11 amino acids from the N-terminus and 1-
96
     5 from the C-terminus can be deleted from said modified human
97
     G-CSF amino acid sequence; and
98
99
     wherein the N-terminus is joined to the C-terminus directly or
100
     through a linker capable of joining the N-terminus to the C-
101
     terminus and having new C- and N-termini at amino acids:
102
103
     38-39
104
                             62-63
                                                 123-124
105
     39-40
                             63-64
                                                 124-125
106
     40 - 41
                             64 - 65
                                                 125-126
107
     41 - 42
                             65-66
                                                 126-127
108
     42 - 43
                             66-67
                                                 128-129
109
     43 - 44
                             67-68
                                                 128-129
110
     45 - 46
                             68-69
                                                 129-130
111
     48-49
                             69-70
                                                 130-131
112
     49-50
                             70-71
                                                 131-132
113
     52 - 53
                             71 - 72
                                                 132-133
114
     53-54
                             91-92
                                                 133-134
115
     54 - 55
                             92-93
                                                 134-135
116
     55-56
                             93-94
                                                 135-136
117
     56-57
                             94-95
                                                 136-137
118
     57-58
                             95-96
                                                 137-138
```

119 120 121 122 123 124 125 126 127	58-59 59-60 60-61 61-62 (II) A poly				96-97 97-98 98-99 99-100					138-139 139-140 140-141 141-142 or 142-143 respectively;					
128	amin	no ad	cid s	seque	ence	of t	the i	formu	ıla:						
129															
130	71 -	D	N-+	mb	C1	m\	m1	<b>Q</b>	T	T	mt	<b>Q</b>	m	** - T	70
131 132	A1a 1	Pro	мес	Thr	GIN 5	Thr	Thr	ser	Leu	ьуs 10	Thr	ser	Trp	vaı	Asn 15
133	<b>-</b>				J					10					10
134	Cys	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa
135	-				20					25					30
136															
137	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Asn	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa
138					35					40					45
139															
140 141	Xaa	Xaa	Xaa	Xaa		Xaa	Xaa	Xaa	Xaa		Xaa	Xaa	Xaa	Xaa	
141					50					55					60
143	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa
144					65					70					75
145															
146	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa
147					80					85					90
148															
149	Xaa	Xaa	Xaa	Xaa		Xaa	Xaa	Xaa	Xaa		Xaa	Xaa	Xaa	Xaa	
150					95					100					105
151 152	Vaa	Pho	Vaa	Vaa	Vaa	V	Xaa	Vaa	Vaa	٧٠٠	Vaa	Vaa	Vaa	Vaa	V
153	Naa	LITE	лаа	лаа	110	Aaa	лаа	лаа	лаа	115	лаа	лаа	лаа	лаа	120
154										.10					120
155	Xaa	Xaa	Xaa	Gln	Gln	Thr	Thr	Leu	Ser	Leu	Ala	Ile	Phe		

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156
                      125
                                          130 (SEQ ID NO:2)
157
158
     wherein Xaa at position 17 is Ser, Lys, Gly, Asp, Met, Gln, or
159
     Arq;
     Xaa at position 18 is Asn, His, Leu, Ile, Phe, Arg, or Gln;
160
161
     Xaa at position 19 is Met, Phe, Ile, Arg, Gly, Ala, or Cys;
162
     Xaa at position 20 is Ile, Cys, Gln, Glu, Arg, Pro, or Ala;
     Xaa at position 21 is Asp, Phe, Lys, Arg, Ala, Gly, Glu, Gln,
163
164
     Asn,
165
          Thr, Ser or Val;
166
     Xaa at position 22 is Glu, Trp, Pro, Ser, Ala, His, Asp, Asn,
167
     Gln,
168
          Leu, Val or Gly;
169
     Xaa at position 23 is Ile, Val, Ala, Gly, Trp, Lys, Phe,
170
          Leu, Ser, or Arg;
171
     Xaa at position 24 is Ile, Gly, Val, Arg, Ser, Phe, or Leu;
172
     Xaa at position 25 is Thr, His, Gly, Gln, Arg, Pro, or Ala;
173
     Xaa at position 26 is His, Thr, Phe, Gly, Arg, Ala, or Trp;
174
     Xaa at position 27 is Leu, Gly, Arq, Thr, Ser, or Ala;
175
     Xaa at position 28 is Lys, Arg, Leu, Gln, Gly, Pro, Val or
176
     Trp;
177
     Xaa at position 29 is Gln, Asn, Leu, Pro, Arg, or Val;
178
     Xaa at position 30 is Pro, His, Thr, Gly, Asp, Gln, Ser, Leu,
179
     or Lys;
180
     Xaa at position 31 is Pro, Asp, Gly, Ala, Arg, Leu, or Gln;
181
     Xaa at position 32 is Leu, Val, Arg, Gln, Asn, Gly, Ala, or
182
     Glu:
183
     Xaa at position 33 is Pro, Leu, Gln, Ala, Thr, or Glu;
     Xaa at position 34 is Leu, Val, Gly, Ser, Lys, Glu, Gln, Thr,
184
185
          Arg, Ala, Phe, Ile or Met;
186
     Xaa at position 35 is Leu, Ala, Gly, Asn, Pro, Gln, or Val;
187
     Xaa at position 36 is Asp, Leu, or Val;
188
     Xaa at position 37 is Phe, Ser, Pro, Trp, or Ile;
     Xaa at position 38 is Asn, or Ala;
189
190
     Xaa at position 40 is Leu, Trp, or Arg;
     Xaa at position 41 is Asn, Cys, Arg, Leu, His, Met, or Pro;
191
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226

227

Val;

- 192 Xaa at position 42 is Gly, Asp, Ser, Cys, Asn, Lys, Thr, Leu, 193 Val, Glu, Phe, Tyr, Ile, Met or Ala; 194 Xaa at position 43 is Glu, Asn, Tyr, Leu, Phe, Asp, Ala, Cys, 195 Gln, Arg, Thr, Gly or Ser; 196 Xaa at position 44 is Asp, Ser, Leu, Arg, Lys, Thr, Met, Trp, 197 Glu, Asn, Gln, Ala or Pro; 198 Xaa at position 45 is Gln, Pro, Phe, Val, Met, Leu, Thr, Lys, 199 Trp, Asp, Asn, Arg, Ser, Ala, Ile, Glu or His; 200 Xaa at position 46 is Asp, Phe, Ser, Thr, Cys, Glu, Asn, Gln, 201 Lys, His, Ala, Tyr, Ile, Val or Gly; 202 Xaa at position 47 is Ile, Gly, Val, Ser, Arg, Pro, or His; 203 Xaa at position 48 is Leu, Ser, Cys, Arg, Ile, His, Phe, Glu, 204 Lys, Thr, Ala, Met, Val or Asn; 205 Xaa at position 49 is Met, Arg, Ala, Gly, Pro, Asn, His, or 206 Asp; 207 Xaa at position 50 is Glu, Leu, Thr, Asp, Tyr, Lys, Asn, Ser, 208 Ala, Ile, Val, His, Phe, Met or Gln; 209 Xaa at position 51 is Asn, Arg, Met, Pro, Ser, Thr, or His; 210 Xaa at position 52 is Asn, His, Arg, Leu, Gly, Ser, or Thr; 211 Xaa at position 53 is Leu, Thr, Ala, Gly, Glu, Pro, Lys, Ser, 212 or Met; 213 Xaa at position 54 is Arg, Asp, Ile, Ser, Val, Thr, Gln, Asn, 214 Lys, His, Ala or Leu; 215 Xaa at position 55 is Arg, Thr, Val, Ser, Leu, or Gly; 216 Xaa at position 56 is Pro, Gly, Cys, Ser, Gln, Glu, Arg, His, 217 Thr, Ala, Tyr, Phe, Leu, Val or Lys; 218 Xaa at position 57 is Asn or Gly; 219 Xaa at position 58 is Leu, Ser, Asp, Arg, Gln, Val, or Cys; 220 Xaa at position 59 is Glu Tyr, His, Leu, Pro, or Arg; 221 Xaa at position 60 is Ala, Ser, Pro, Tyr, Asn, or Thr; 222 Xaa at position 61 is Phe, Asn, Glu, Pro, Lys, Arg, or Ser; 223 Xaa at position 62 is Asn, His, Val, Arg, Pro, Thr, Asp, or 224 Ile:

Xaa at position 63 is Arg, Tyr, Trp, Lys, Ser, His, Pro, or

251

Xaa at position 64 is Ala, Asn, Pro, Ser, or Lys;

262

263

- 228 Xaa at position 65 is Val, Thr, Pro, His, Leu, Phe, or Ser; 229 Xaa at position 66 is Lys, Ile, Arg, Val, Asn, Glu, or Ser; 230 Xaa at position 67 is Ser, Ala, Phe, Val, Gly, Asn, Ile, Pro, 231 or His; 232 Xaa at position 68 is Leu, Val, Trp, Ser, Ile, Phe, Thr, or 233 234 Xaa at position 69 is Gln, Ala, Pro, Thr, Glu, Arg, Trp, Gly, 235 or Leu; Xaa at position 70 is Asn, Leu, Val, Trp, Pro, or Ala; 236 237 Xaa at position 71 is Ala, Met, Leu, Pro, Arg, Glu, Thr, Gln, 238 Trp, or Asn; 239 Xaa at position 72 is Ser, Glu, Met, Ala, His, Asn, Arg, or 240 Asp; 241 Xaa at position 73 is Ala, Glu, Asp, Leu, Ser, Gly, Thr, or 242 Arq; 243 Xaa at position 74 is Ile, Met, Thr, Pro, Arg, Gly, Ala; 244 Xaa at position 75 is Glu, Lys, Gly, Asp, Pro, Trp, Arg, Ser, 245 Gln, or Leu; 246 Xaa at position 76 is Ser, Val, Ala, Asn, Trp, Glu, Pro, Gly, 247 or Asp; 248 Xaa at position 77 is Ile, Ser, Arg, Thr, or Leu; 249 Xaa at position 78 is Leu, Ala, Ser, Glu, Phe, Gly, or Arg; 250 Xaa at position 79 is Lys, Thr, Asn, Met, Arg, Ile, Gly, or 251 Asp; 252 Xaa at position 80 is Asn, Trp, Val, Gly, Thr, Leu, Glu, or 253 254 Xaa at position 81 is Leu, Gln, Gly, Ala, Trp, Arg, Val, or 255 Lys; 256 Xaa at position 82 is Leu, Gln, Lys, Trp, Arg, Asp, Glu, Asn, 257 His, Thr, Ser, Ala, Tyr, Phe, Ile, Met or Val; 258 Xaa at position 83 is Pro, Ala, Thr, Trp, Arq, or Met; 259 Xaa at position 84 is Cys, Glu, Gly, Arg, Met, or Val; 260 Xaa at position 85 is Leu, Asn, Val, or Gln;

Xaa at position 86 is Pro, Cys, Arg, Ala, or Lys;

Xaa at position 88 is Ala, Lys, Arg, Val, or Trp;

Xaa at position 87 is Leu, Ser, Trp, or Gly;

- 264 Xaa at position 89 is Thr, Asp, Cys, Leu, Val, Glu, His, Asn,
- 265 or Ser;
- 266 Xaa at position 90 is Ala, Pro, Ser, Thr, Gly, Asp, Ile, or
- 267 Met;
- 268 Xaa at position 91 is Ala, Pro, Ser, Thr, Phe, Leu, Asp, or
- 269 His;
- 270 Xaa at position 92 is Pro, Phe, Arg, Ser, Lys, His, Ala, Gly,
- 271 Ile or Leu;
- 272 Xaa at position 93 is Thr, Asp, Ser, Asn, Pro, Ala, Leu, or
- 273 Arg;
- 274 Xaa at position 94 is Arg, Ile, Ser, Glu, Leu, Val, Gln, Lys,
- 275 His, Ala, or Pro;
- 276 Xaa at position 95 is His, Gln, Pro, Arg, Val, Leu, Gly, Thr,
- 277 Asn, Lys, Ser, Ala, Trp, Phe, Ile, or Tyr;
- 278 Xaa at position 96 is Pro, Lys, Tyr, Gly, Ile, or Thr;
- 279 Xaa at position 97 is Ile, Val, Lys, Ala, or Asn;
- 280 Xaa at position 98 is His, Ile, Asn, Leu, Asp, Ala, Thr,
- 281 Glu, Gln, Ser, Phe, Met, Val, Lys, Arg, Tyr or Pro;
- 282 Xaa at position 99 is Ile, Leu, Arg, Asp, Val, Pro, Gln,
- 283 Gly, Ser, Phe, or His;
- 284 Xaa at position 100 is Lys, Tyr, Leu, His, Arg, Ile, Ser, Gln,
- 285 or Pro;
- 286 Xaa at position 101 is Asp, Pro, Met, Lys, His, Thr, Val,
- Tyr, Glu, Asn, Ser, Ala, Gly, Ile, Leu, or Gln;
- 288 Xaa at position 102 is Gly, Leu, Glu, Lys, Ser, Tyr, or Pro;
- 289 Xaa at position 103 is Asp, or Ser;
- 290 Xaa at position 104 is Trp, Val, Cys, Tyr, Thr, Met, Pro, Leu,
- 291 Gln, Lys, Ala, Phe, or Gly;
- 292 Xaa at position 105 is Asn, Pro, Ala, Phe, Ser, Trp, Gln, Tyr,
- Leu, Lys, Ile, Asp, or His;
- 294 Xaa at position 106 is Glu, Ser, Ala, Lys, Thr, Ile, Gly, or
- 295 Pro;
- 296 Xaa at position 108 is Arg, Lys, Asp, Leu, Thr, Ile, Gln, His,
- 297 Ser, Ala or Pro;
- 298 Xaa at position 109 is Arg, Thr, Pro, Glu, Tyr, Leu, Ser, or
- 299 Gly;

334

335

- 300 Xaa at position 110 is Lys, Ala, Asn, Thr, Leu, Arg, Gln, His, 301 Glu, Ser, or Trp; 302 Xaa at position 111 is Leu, Ile, Arg, Asp, or Met; 303 Xaa at position 112 is Thr, Val, Gln, Tyr, Glu, His, Ser, or 304 Phe: 305 Xaa at position 113 is Phe, Ser, Cys, His, Gly, Trp, Tyr, Asp, Lys, Leu, Ile, Val or Asn; 306 307 Xaa at position 114 is Tyr, Cys, His, Ser, Trp, Arg, or Leu; 308 Xaa at position 115 is Leu, Asn, Val, Pro, Arg, Ala, His, Thr, 309 Trp, or Met; 310 Xaa at position 116 is Lys, Leu, Pro, Thr, Met, Asp, Val, Glu, 311 Arg, Trp, Ser, Asn, His, Ala, Tyr, Phe, Gln, or Ile; 312 Xaa at position 117 is Thr, Ser, Asn, Ile, Trp, Lys, or Pro; 313 Xaa at position 118 is Leu, Ser, Pro, Ala, Glu, Cys, Asp, or 314 Tyr; 315 Xaa at position 119 is Glu, Ser, Lys, Pro, Leu, Thr, Tyr, or 316 317 Xaa at position 120 is Asn, Ala, Pro, Leu, His, Val, or Gln; 318 Xaa at position 121 is Ala, Ser, Ile, Asn, Pro, Lys, Asp, or 319 Gly; 320 Xaa at position 122 is Gln, Ser, Met, Trp, Arg, Phe, Pro, His, 321 Ile, Tyr, or Cys; 322 Xaa at position 123 is Ala, Met, Glu, His, Ser, Pro, Tyr, or 323 Leu, 324 325 wherein from 1 to 14 amino acids can optionally be deleted 326 from the N-terminus and/or from 1 to 15 amino acids can 327 optionally be deleted from the C-terminus of said modified 328 human IL-3 amino acid sequence; and wherein from 0 to 44 of 329 the amino acids designated by Xaa are different from the 330 corresponding amino acids of native (1-133) human interleukin-331 3; and 332

wherein the N-terminus is joined to the C-terminus directly or

through a linker (L2) capable of joining the N-terminus to the

C-terminus and having new C- and N-termini at amino acids:

26-27	49-50	83-84
27-28	50-51	84-85
28-29	51-52	85-86
29-30	52-53	86-87
30-31	53-54	87-88
31-32	54-55	88-89
32-33	64-65	89-90
33-34	65-66	90-91
34-35	66-67	91-92
35-36	67-68	92-93
36-37	68-69	97-98
37-38	69-70	98-99
38-39	70-71	99-100
39-40	71-72	100-101
40-41	72-73	101-102
41-42	82-83	102-103
		or 103-104
		respectively;

(III) A polypeptide comprising; a modified human c-mpl ligand amino acid sequence of the formula:

SerProAlaProProAlaCysAspLeuArgValLeuSerLysLeuLeuArgAspSer 1 5 10 15

HisValLeuHisSerArgLeuSerGlnCysProGluValHisProLeuProThrPro 20 25 30 35

ValLeuLeuProAlaValAspPheSerLeuGlyGluTrpLysThrGlnMetGluGlu 40 45 50 55

ThrLysAlaGlnAspIleLeuGlyAlaValThrLeuLeuGluGlyValMetAla
60 65 70 75

AlaArgGlyGlnLeuGlyProThrCysLeuSerSerLeuLeuGlyGlnLeuSerGly 80 85 90 95

GlnValArgLeuLeuGlyAlaLeuGlnSerLeuLeuGlyThrGlnXaaXaaXaa 100 105 110

XaaGlyArgThrThrAlaHisLysAspProAsnAlaIlePheLeuSerPheGlnHis 115 120 125 130

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362
363
     LeuLeuArgGlyLysValArgPheLeuMetLeuValGlyGlySerThrLeuCysVal
364
                        140
        135
                                       145
                                                       150
365
366
     Arg (SEQ ID NO:256)
367
     153
368
369
     wherein
370
371
     Xaa at position 112 is deleted or Leu, Ala, Val, Ile, Pro,
372
     Phe, Trp, or Met;
373
     Xaa at position 113 is deleted or Pro, Phe, Ala, Val, Leu,
374
     Ile, Trp, or Met;
375
     Xaa at position 114 is deleted or Pro, Phe, Ala, Val, Leu,
376
     Ile, Trp, or Met;
377
     Xaa at position 115 is deleted or Gln, Gly, Ser, Thr, Tyr, or
378
     Asn; and
379
380
     wherein the N-terminus is joined to the C-terminus directly or
381
     through a linker (L2) capable of joining the N-terminus to the
382
     C-terminus and having new C- and N-termini at amino acids:
383
```

52-53	108-109
53-54	109-110
54-55	110-111
55-56	111-112
56-57	112-113
57-58	113-114
58-59	114-115
59-60	115-116
78-79	116-117
79-80	117-118
80-81	118-119
81-82	119-120
82-83	120-121
83-84	121-122
84-85	122-123
85-86	123-124
86-87	124-125
87-88	125-126
88-89	126-127

						or 1	27-1	28							
						resp	ecti	vely	;						
384															
385				_							,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,				_
386							_		-	a mo	odifi	ied l	numar	ı IL-	-3
387	amıı	no a	cid s	seque	ence	of t	the i	torm	ıla:						
388															
389 390	7.1.5	Dro	Mo+		Cln	Th v	Πh∽	Cor	T 011	T	መኤኤ	C 0 m	Пъъ	17 n l	λαν
391	1	PIO	мес	TIIL	5	IIIL	Inr	ser	Leu		Inr	ser	Trp	val	
392	1				J					10					15
393	Cvs	Xaa	Xaa	Хаа	Xaa	Xaa	Yaa	Хаа	Yaa	Yaa	Хаа	Xaa	Xaa	Yaa	Yaa
394	Cyb	naa	naa	naa	20	naa	naa	nuu	naa	25	Naa	naa	Nau	naa	30
395					20					23					30
396	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Asn	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa
397					35					40					45
398															
399	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa
400					50					55					60
401															
402	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa
403					65					70					75
404															
405	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa
406					80					85					90
407															
408	Xaa	Xaa	Xaa	Xaa		Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	Xaa	
409					95					100					105
410															
411	Xaa	Phe	Xaa	Xaa		Xaa	Xaa	Xaa	Xaa		Xaa	Xaa	Xaa	Xaa	
412					110					115					120
413				<b>~</b> 1	<b>.</b>		_,	_	_	_					
414	хаа	хаа	хаа	GIn		Thr	Thr	Leu	Ser						
415					125					130	(SE)	QI Ç	NO:2	۷)	
416															

452

417 wherein Xaa at position 17 is Ser, Lys, Gly, Asp, Met, Gln, or 418 419 Xaa at position 18 is Asn, His, Leu, Ile, Phe, Arg, or Gln; 420 Xaa at position 19 is Met, Phe, Ile, Arg, Gly, Ala, or Cys; 421 Xaa at position 20 is Ile, Cys, Gln, Glu, Arg, Pro, or Ala; 422 Xaa at position 21 is Asp, Phe, Lys, Arg, Ala, Gly, Glu, Gln, 423 Asn, Thr, Ser or Val; 424 Xaa at position 22 is Glu, Trp, Pro, Ser, Ala, His, Asp, Asn, 425 Gln, Leu, Val or Gly; 426 Xaa at position 23 is Ile, Val, Ala, Gly, Trp, Lys, Phe, 427 Leu, Ser, or Arg; 428 Xaa at position 24 is Ile, Gly, Val, Arg, Ser, Phe, or Leu; 429 Xaa at position 25 is Thr, His, Gly, Gln, Arg, Pro, or Ala; 430 Xaa at position 26 is His, Thr, Phe, Gly, Arg, Ala, or Trp; 431 Xaa at position 27 is Leu, Gly, Arg, Thr, Ser, or Ala; 432 Xaa at position 28 is Lys, Arg, Leu, Gln, Gly, Pro, Val or 433 Trp; 434 Xaa at position 29 is Gln, Asn, Leu, Pro, Arg, or Val; 435 Xaa at position 30 is Pro, His, Thr, Gly, Asp, Gln, Ser, Leu, 436 or Lys; 437 Xaa at position 31 is Pro, Asp, Gly, Ala, Arg, Leu, or Gln; 438 Xaa at position 32 is Leu, Val, Arg, Gln, Asn, Gly, Ala, or 439 Glu; 440 Xaa at position 33 is Pro, Leu, Gln, Ala, Thr, or Glu; 441 Xaa at position 34 is Leu, Val, Gly, Ser, Lys, Glu, Gln, Thr, 442 Arg, Ala, Phe, Ile or Met; 443 Xaa at position 35 is Leu, Ala, Gly, Asn, Pro, Gln, or Val; 444 Xaa at position 36 is Asp, Leu, or Val; 445 Xaa at position 37 is Phe, Ser, Pro, Trp, or Ile; 446 Xaa at position 38 is Asn, or Ala; 447 Xaa at position 40 is Leu, Trp, or Arg; 448 Xaa at position 41 is Asn, Cys, Arg, Leu, His, Met, or Pro; 449 Xaa at position 42 is Gly, Asp, Ser, Cys, Asn, Lys, Thr, Leu, 450 Val, Glu, Phe, Tyr, Ile, Met or Ala;

Xaa at position 43 is Glu, Asn, Tyr, Leu, Phe, Asp, Ala, Cys,

Gln, Arg, Thr, Gly or Ser;

453 Xaa at position 44 is Asp, Ser, Leu, Arg, Lys, Thr, Met, Trp, 454 Glu, Asn, Gln, Ala or Pro; Xaa at position 45 is Gln, Pro, Phe, Val, Met, Leu, Thr, Lys, 455 456 Trp, Asp, Asn, Arg, Ser, Ala, Ile, Glu or His; 457 Xaa at position 46 is Asp, Phe, Ser, Thr, Cys, Glu, Asn, Gln, 458 Lys, His, Ala, Tyr, Ile, Val or Gly; 459 Xaa at position 47 is Ile, Gly, Val, Ser, Arg, Pro, or His; 460 Xaa at position 48 is Leu, Ser, Cys, Arg, Ile, His, Phe, Glu, Lys, Thr, Ala, Met, Val or Asn; 461 462 Xaa at position 49 is Met, Arg, Ala, Gly, Pro, Asn, His, or 463 Asp; 464 Xaa at position 50 is Glu, Leu, Thr, Asp, Tyr, Lys, Asn, Ser, 465 Ala, Ile, Val, His, Phe, Met or Gln; 466 Xaa at position 51 is Asn, Arg, Met, Pro, Ser, Thr, or His; 467 Xaa at position 52 is Asn, His, Arg, Leu, Gly, Ser, or Thr; 468 Xaa at position 53 is Leu, Thr, Ala, Gly, Glu, Pro, Lys, Ser, 469 or Met; 470 Xaa at position 54 is Arg, Asp, Ile, Ser, Val, Thr, Gln, Asn, 471 Lys, His, Ala or Leu; 472 Xaa at position 55 is Arg, Thr, Val, Ser, Leu, or Gly; 473 Xaa at position 56 is Pro, Gly, Cys, Ser, Gln, Glu, Arg, His, 474 Thr, Ala, Tyr, Phe, Leu, Val or Lys; 475 Xaa at position 57 is Asn or Gly; 476 Xaa at position 58 is Leu, Ser, Asp, Arg, Gln, Val, or Cys; 477 Xaa at position 59 is Glu Tyr, His, Leu, Pro, or Arg; 478 Xaa at position 60 is Ala, Ser, Pro, Tyr, Asn, or Thr; 479 Xaa at position 61 is Phe, Asn, Glu, Pro, Lys, Arg, or Ser; 480 Xaa at position 62 is Asn, His, Val, Arg, Pro, Thr, Asp, or 481 Ile; 482 Xaa at position 63 is Arg, Tyr, Trp, Lys, Ser, His, Pro, or 483 Val; 484 Xaa at position 64 is Ala, Asn, Pro, Ser, or Lys; 485 Xaa at position 65 is Val, Thr, Pro, His, Leu, Phe, or Ser; 486 Xaa at position 66 is Lys, Ile, Arg, Val, Asn, Glu, or Ser; 487 Xaa at position 67 is Ser, Ala, Phe, Val, Gly, Asn, Ile, Pro, 488 or His;

489 Xaa at position 68 is Leu, Val, Trp, Ser, Ile, Phe, Thr, or 490 His; 491 Xaa at position 69 is Gln, Ala, Pro, Thr, Glu, Arg, Trp, Gly, 492 or Leu; 493 Xaa at position 70 is Asn, Leu, Val, Trp, Pro, or Ala; 494 Xaa at position 71 is Ala, Met, Leu, Pro, Arg, Glu, Thr, Gln, 495 Trp, or Asn; 496 Xaa at position 72 is Ser, Glu, Met, Ala, His, Asn, Arg, or 497 Asp; 498 Xaa at position 73 is Ala, Glu, Asp, Leu, Ser, Gly, Thr, or 499 500 Xaa at position 74 is Ile, Met, Thr, Pro, Arg, Gly, Ala; 501 Xaa at position 75 is Glu, Lys, Gly, Asp, Pro, Trp, Arg, Ser, 502 Gln, or Leu; 503 Xaa at position 76 is Ser, Val, Ala, Asn, Trp, Glu, Pro, Gly, 504 or Asp; 505 Xaa at position 77 is Ile, Ser, Arg, Thr, or Leu; 506 Xaa at position 78 is Leu, Ala, Ser, Glu, Phe, Gly, or Arg; 507 Xaa at position 79 is Lys, Thr, Asn, Met, Arg, Ile, Gly, or 508 Asp; 509 Xaa at position 80 is Asn, Trp, Val, Gly, Thr, Leu, Glu, or 510 511 Xaa at position 81 is Leu, Gln, Gly, Ala, Trp, Arq, Val, or 512 Lys; 513 Xaa at position 82 is Leu, Gln, Lys, Trp, Arg, Asp, Glu, Asn, 514 His, Thr, Ser, Ala, Tyr, Phe, Ile, Met or Val; 515 Xaa at position 83 is Pro, Ala, Thr, Trp, Arg, or Met; 516 Xaa at position 84 is Cys, Glu, Gly, Arg, Met, or Val; Xaa at position 85 is Leu, Asn, Val, or Gln; 517 518 Xaa at position 86 is Pro, Cys, Arg, Ala, or Lys; 519 Xaa at position 87 is Leu, Ser, Trp, or Gly; 520 Xaa at position 88 is Ala, Lys, Arg, Val, or Trp; 521 Xaa at position 89 is Thr, Asp, Cys, Leu, Val, Glu, His, Asn, 522 or Ser; 523 Xaa at position 90 is Ala, Pro, Ser, Thr, Gly, Asp, Ile, or

524

Met;

- 525 Xaa at position 91 is Ala, Pro, Ser, Thr, Phe, Leu, Asp, or
- 526 His;
- 527 Xaa at position 92 is Pro, Phe, Arg, Ser, Lys, His, Ala, Gly,
- 528 Ile or Leu;
- 529 Xaa at position 93 is Thr, Asp, Ser, Asn, Pro, Ala, Leu, or
- 530 Arg
- 531 Xaa at position 94 is Arg, Ile, Ser, Glu, Leu, Val, Gln, Lys,
- 532 His, Ala, or Pro;
- 533 Xaa at position 95 is His, Gln, Pro, Arg, Val, Leu, Gly, Thr,
- 534 Asn, Lys, Ser, Ala, Trp, Phe, Ile, or Tyr;
- 535 Xaa at position 96 is Pro, Lys, Tyr, Gly, Ile, or Thr;
- 536 Xaa at position 97 is Ile, Val, Lys, Ala, or Asn;
- 537 Xaa at position 98 is His, Ile, Asn, Leu, Asp, Ala, Thr,
- Glu, Gln, Ser, Phe, Met, Val, Lys, Arg, Tyr or Pro;
- 539 Xaa at position 99 is Ile, Leu, Arg, Asp, Val, Pro, Gln,
- Gly, Ser, Phe, or His;
- 541 Xaa at position 100 is Lys, Tyr, Leu, His, Arg, Ile, Ser, Gln,
- 542 or Pro;
- 543 Xaa at position 101 is Asp, Pro, Met, Lys, His, Thr, Val,
- 544 Tyr, Glu, Asn, Ser, Ala, Gly, Ile, Leu, or Gln;
- 545 Xaa at position 102 is Gly, Leu, Glu, Lys, Ser, Tyr, or Pro;
- 546 Xaa at position 103 is Asp, or Ser;
- 547 Xaa at position 104 is Trp, Val, Cys, Tyr, Thr, Met, Pro, Leu,
- Gln, Lys, Ala, Phe, or Gly;
- 549 Xaa at position 105 is Asn, Pro, Ala, Phe, Ser, Trp, Gln, Tyr,
- Leu, Lys, Ile, Asp, or His;
- 551 Xaa at position 106 is Glu, Ser, Ala, Lys, Thr, Ile, Gly, or
- 552 Pro;
- 553 Xaa at position 108 is Arg, Lys, Asp, Leu, Thr, Ile, Gln, His,
- 554 Ser, Ala or Pro;
- 555 Xaa at position 109 is Arg, Thr, Pro, Glu, Tyr, Leu, Ser, or
- 556 Gly;
- 557 Xaa at position 110 is Lys, Ala, Asn, Thr, Leu, Arg, Gln, His,
- 558 Glu, Ser, or Trp;
- 559 Xaa at position 111 is Leu, Ile, Arg, Asp, or Met;

560 Xaa at position 112 is Thr, Val, Gln, Tyr, Glu, His, Ser, or 561 Phe; 562 Xaa at position 113 is Phe, Ser, Cys, His, Gly, Trp, Tyr, Asp, 563 Lys, Leu, Ile, Val or Asn; 564 Xaa at position 114 is Tyr, Cys, His, Ser, Trp, Arg, or Leu; 565 Xaa at position 115 is Leu, Asn, Val, Pro, Arg, Ala, His, Thr, 566 Trp, or Met; 567 Xaa at position 116 is Lys, Leu, Pro, Thr, Met, Asp, Val, Glu, 568 Arg, Trp, Ser, Asn, His, Ala, Tyr, Phe, Gln, or Ile; 569 Xaa at position 117 is Thr, Ser, Asn, Ile, Trp, Lys, or Pro; 570 Xaa at position 118 is Leu, Ser, Pro, Ala, Glu, Cys, Asp, or 571 572 Xaa at position 119 is Glu, Ser, Lys, Pro, Leu, Thr, Tyr, or 573 Arq; 574 Xaa at position 120 is Asn, Ala, Pro, Leu, His, Val, or Gln; 575 Xaa at position 121 is Ala, Ser, Ile, Asn, Pro, Lys, Asp, or 576 577 Xaa at position 122 is Gln, Ser, Met, Trp, Arg, Phe, Pro, His, 578 Ile, Tyr, or Cys; 579 Xaa at position 123 is Ala, Met, Glu, His, Ser, Pro, Tyr, or 580 Leu, 581 582 wherein from 1 to 14 amino acids can optionally be deleted 583 from the N-terminus and/or from 1 to 15 amino acids can 584 optionally be deleted from the C-terminus of said modified 585 human IL-3 amino acid sequence; and wherein from 1 to 44 of 586 the amino acids designated by Xaa are different from the 587 corresponding amino acids of native (1-133) human interleukin-588 3, and 589 590 (V) a colony stimulating factor; 591 592 and wherein L1 is a linker capable of linking R1 to R2 593 594 with the proviso that at least R1 or R2 is selected from 595 the polypeptide of formula (I) , (II), or (III); and

said hematopoietic protein can optionally be immediately preceded by  $(methionine^{-1})$ ,  $(alanine^{-1})$  or  $(methionine^{-2})$ , alanine $^{-1}$ ).

wherein the polypeptide of (IV) is selected from the from the group consisting of: Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys

The hematopoietic protein as recited in claim 1

Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala Glu

Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu

Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly

Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala

Thr Ala Ala Pro Ser Arq His Pro Ile Ile Lys Ala Gly Asp

Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu

Glu Gln Ala Gln Glu Gln Gln (SEQ ID NO:225);

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys

Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu

Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu

Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly

Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala

Thr Ala Ala Pro Ser Arg His Pro Ile Ile Lys Ala Gly Asp

Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu

Glu Gln Ala Gln Glu Gln Gln (SEQ ID NO:226);

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys

Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arq His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln (SEQ ID NO:227); and 

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arq Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln (SEQ ID NO:228).

5.

group consisting of:

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Glu Arg Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu

Glu Gln Ala Gln Glu Gln Gln (SEQ ID NO:225);

The hematopoietic protein as recited in claim 2

wherein the polypeptide of (IV) is selected from the from the

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln (SEQ ID NO:226); Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln (SEQ ID NO:227); and Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu 

Gln Ala Gln Glu Gln Gln (SEQ ID NO:228).

6. The hematopoietic protein as recited in claim 3 wherein the polypeptide of (IV) is selected from the from the group consisting of: Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln (SEQ ID NO:225); Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln (SEO ID NO:226); Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser Glu 

Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu

Leu Ala Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly

```
47
    Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala
48
49
    Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp
50
51
    Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu
52
53
    Glu Gln Ala Gln Glu Gln (SEQ ID NO:227); and
54
55
    Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg
56
    Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp
57
    Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu
58
    Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile
59
    Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr
60
    Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp
61
    Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu
62
    Gln Ala Gln Glu Gln (SEQ ID NO:228).
1
             A hematopoietic protein comprising; an amino acid sequence
2
    of the formula:
3
```

 $R_1-L_1-R_2$ ,  $R_2-L_1-R_1$ ,  $R_1-R_2$ , or  $R_2-R_1$ 

wherein R<sub>1</sub> is a polypeptide comprising; a modified human G-CSF amino acid sequence of the formula:

Xaa Xaa Xaa Gly Pro Ala Ser Ser Leu Pro Gln Ser Xaa

Leu Leu Xaa Xaa Xaa Glu Gln Val Xaa Lys Xaa Gln Gly Xaa Gly

30 40

Ala Xaa Leu Gln Glu Xaa Leu Xaa Ala Thr Tyr Lys Leu Xaa Xaa 17

Xaa Glu Xaa Xaa Val Xaa Xaa Gly His Ser Xaa Gly Ile Pro Trp 20

21 60

22 Ala Pro Leu Ser Ser Xaa Pro Ser Xaa Ala Leu Xaa Leu Ala Gly 

25 Xaa Leu Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu

```
26
27
        90
                                                  100
28
    Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu
29
30
                             110
31
    Xaa Thr Leu Gln Xaa Asp Val Ala Asp Phe Ala Xaa Thr Ile Trp
32
33
34
    Gln Gln Met Glu Xaa Xaa Gly Met Ala Pro Ala Leu Gln Pro Thr
35
36
                             140
37
    Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Xaa Gln Xaa Xaa Ala
38
39
        150
                                                  160
40
    Gly Gly Val Leu Val Ala Ser Xaa Leu Gln Xaa Phe Leu Xaa Xaa
41
42
                             170
43
    Ser Tyr Arg Val Leu Xaa Xaa Leu Ala Gln Pro (SEQ ID NO:1)
44
45
    wherein
46
47
    Xaa at position 1 is Thr, Ser, Arg, Tyr or Gly;
48
    Xaa at position 2 is Pro or Leu;
49
    Xaa at position 3 is Leu, Arg, Tyr or Ser;
50
    Xaa at position 13 is Phe, Ser, His, Thr or Pro;
51
    Xaa at position 16 is Lys, Pro, Ser, Thr or His;
52
    Xaa at position 17 is Cys, Ser, Gly, Ala, Ile, Tyr or
53
    Xaa at position 18 is Leu, Thr, Pro, His, Ile or Cys;
54
    Xaa at position 22 is Arg, Tyr, Ser, Thr or Ala;
55
    Xaa at position 24 is Ile, Pro, Tyr or Leu;
    Xaa at position 27 is Asp, or Gly;
56
57
    Xaa at position 30 is Ala, Ile, Leu or Gly;
58
    Xaa at position 34 is Lys or Ser;
59
    Xaa at position 36 is Cys or Ser;
60
    Xaa at position 42 is Cys or Ser;
61
    Xaa at position 43 is His, Thr, Gly, Val, Lys, Trp, Ala,
62
         Arg, Cys, or Leu;
63
    Xaa at position 44 is Pro, Gly, Arg, Asp, Val, Ala, His,
64
         Trp, Gln, or Thr;
65
    Xaa at position 46 is Glu, Arg, Phe, Arg, Ile or Ala;
66
    Xaa at position 47 is Leu or Thr;
    Xaa at position 49 is Leu, Phe, Arg or Ser;
67
68
    Xaa at position 50 is Leu, Ile, His, Pro or Tyr;
69
    Xaa at position 54 is Leu or His;
70
    Xaa at position 64 is Cys or Ser;
    Xaa at position 67 is Gln, Lys, Leu or Cys;
71
72
    Xaa at position 70 is Gln, Pro, Leu, Arg or Ser;
```

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73
     Xaa at position 74 is Cys or Ser;
74
     Xaa at position 104 is Asp, Gly or Val;
75
     Xaa at position 108 is Leu, Ala, Val, Arg, Trp, Gln or
76
          Glv;
77
     Xaa at position 115 is Thr, His, Leu or Ala;
78
     Xaa at position 120 is Gln, Gly, Arg, Lys or His
     Xaa at position 123 is Glu, Arg, Phe or Thr
79
 80
     Xaa at position 144 is Phe, His, Arg, Pro, Leu, Gln or
 81
          Glu;
 82
     Xaa at position 146 is Arg or Gln;
83
     Xaa at position 147 is Arg or Gln;
 84
     Xaa at position 156 is His, Gly or Ser;
 85
     Xaa at position 159 is Ser, Arg, Thr, Tyr, Val or Gly;
     Xaa at position 162 is Glu, Leu, Gly or Trp;
 86
 87
     Xaa at position 163 is Val, Gly, Arg or Ala;
 88
     Xaa at position 169 is Arg, Ser, Leu, Arg or Cys;
 89
     Xaa at position 170 is His, Arg or Ser,
90
91
     wherein optionally 1-11 amino acids from the N-terminus and 1-
92
     5 from the C-terminus can be deleted from said modified human
93
     G-CSF amino acid sequence; and
94
95
     wherein the N-terminus is joined to the C-terminus directly or
96
     through a linker capable of joining the N-terminus to the C-
97
     terminus and having new C- and N-termini at amino acids:
98
99
100
     38 - 39
                             62-63
                                                 123-124
101
     39-40
                             63-64
                                                 124-125
102
     40 - 41
                             64 - 65
                                                 125-126
103
     41 - 42
                             65-66
                                                 126-127
104
     42-43
                             66-67
                                                 128-129
105
     43-44
                             67-68
                                                 128-129
106
     45-46
                             68-69
                                                 129-130
107
     48 - 49
                             69-70
                                                 130-131
108
     49-50
                             70-71
                                                 131-132
109
     52-53
                             71-72
                                                 132 - 133
110
     53-54
                             91-92
                                                 133-134
111
     54-55
                             92-93
                                                 134-135
112
     55-56
                             93 - 94
                                                 135-136
113
     56-57
                             94-95
                                                 136-137
     57-58
114
                                                 137-138
                             95-96
115
     58-59
                             96-97
                                                 138-139
116
     59-60
                             97-98
                                                 139-140
117
     60-61
                             98-99
                                                 140-141
118
     61-62
                             99-100
                                                 141-142
```

119 120 121				or 142-143 respectively,	
122 123	where	in R2 is a pc	olypeptide compr	ising; a modified hu	ıman
124			e of the formul		
125		-			
126	Ala Pro Me	t Thr Gln Thr	Thr Ser Leu Ly	s Thr Ser Trp Val As	sn
127	1	5	10	15	5
128					
129	Cys Xaa Xa	a Xaa Xaa Xaa	Xaa Xaa Xaa Xa	a Xaa Xaa Xaa Xaa X	aa
130		20	25	30	)
131					
132	Xaa Xaa Xa	a Xaa Xaa Xaa	Xaa Xaa Asn Xa	a Xaa Xaa Xaa Xaa Xa	aa
133		35	40	45	5
134					
135	Xaa Xaa Xa			a Xaa Xaa Xaa Xaa Xa	
136		50	55	60	)
137	W W W-		., ., ., .,		
138	xaa xaa xa			a Xaa Xaa Xaa Xaa Xa	
139 140		65	70	75	0
141	Yaa Yaa Ya	a Yaa Yaa Yaa	Yaa Yaa Yaa Ya	a Xaa Xaa Xaa Xaa Xa	
142	naa naa na	80	85		
143			00	30	,
144	Xaa Xaa Xa	a Xaa Xaa Xaa	Xaa Xaa Xaa Xa	a Xaa Xaa Xaa Xaa Xa	aa
145		95	10		
146					
147	Xaa Phe Xa	a Xaa Xaa Xaa	. Xaa Xaa Xaa Xa	a Xaa Xaa Xaa Xaa Xa	aa
148		110	11	5 12	20
149					
150	Xaa Xaa Xa	a Gln Gln Thr	Thr Leu Ser Le	u Ala Ile Phe	
151		125	13	0 (SEQ ID NO:2)	
152					
153	wherein Xa	a at position	17 is Ser, Lys	, Gly, Asp, Met, Glr	n, or
154	Arg;				

155 Xaa at position 18 is Asn, His, Leu, Ile, Phe, Arg, or Gln; 156 Xaa at position 19 is Met, Phe, Ile, Arg, Gly, Ala, or Cys; 157 Xaa at position 20 is Ile, Cys, Gln, Glu, Arg, Pro, or Ala; 158 Xaa at position 21 is Asp, Phe, Lys, Arg, Ala, Gly, Glu, Gln, 159 Asn, Thr, Ser or Val; 160 Xaa at position 22 is Glu, Trp, Pro, Ser, Ala, His, Asp, Asn, 161 Gln, Leu, Val or Gly; 162 Xaa at position 23 is Ile, Val, Ala, Gly, Trp, Lys, Phe, Leu, Ser, or Arg; 163 164 Xaa at position 24 is Ile, Gly, Val, Arg, Ser, Phe, or Leu; 165 Xaa at position 25 is Thr, His, Gly, Gln, Arg, Pro, or Ala; 166 Xaa at position 26 is His, Thr, Phe, Gly, Arg, Ala, or Trp; 167 Xaa at position 27 is Leu, Gly, Arg, Thr, Ser, or Ala; 168 Xaa at position 28 is Lys, Arg, Leu, Gln, Gly, Pro, Val or 169 Trp; 170 Xaa at position 29 is Gln, Asn, Leu, Pro, Arg, or Val; 171 Xaa at position 30 is Pro, His, Thr, Gly, Asp, Gln, Ser, Leu, 172 or Lys; Xaa at position 31 is Pro, Asp, Gly, Ala, Arg, Leu, or Gln; 173 174 Xaa at position 32 is Leu, Val, Arg, Gln, Asn, Gly, Ala, or 175 Glu; 176 Xaa at position 33 is Pro, Leu, Gln, Ala, Thr, or Glu; 177 Xaa at position 34 is Leu, Val, Gly, Ser, Lys, Glu, Gln, Thr, 178 Arg, Ala, Phe, Ile or Met; 179 Xaa at position 35 is Leu, Ala, Gly, Asn, Pro, Gln, or Val; 180 Xaa at position 36 is Asp, Leu, or Val; 181 Xaa at position 37 is Phe, Ser, Pro, Trp, or Ile; 182 Xaa at position 38 is Asn, or Ala; 183 Xaa at position 40 is Leu, Trp, or Arg; 184 Xaa at position 41 is Asn, Cys, Arg, Leu, His, Met, or Pro; 185 Xaa at position 42 is Gly, Asp, Ser, Cys, Asn, Lys, Thr, Leu, 186 Val, Glu, Phe, Tyr, Ile, Met or Ala; 187 Xaa at position 43 is Glu, Asn, Tyr, Leu, Phe, Asp, Ala, Cys, 188 Gln, Arg, Thr, Gly or Ser; 189 Xaa at position 44 is Asp, Ser, Leu, Arg, Lys, Thr, Met, Trp,

Glu, Asn, Gln, Ala or Pro;

190

191 Xaa at position 45 is Gln, Pro, Phe, Val, Met, Leu, Thr, Lys, 192 Trp, Asp, Asn, Arg, Ser, Ala, Ile, Glu or His; 193 Xaa at position 46 is Asp, Phe, Ser, Thr, Cys, Glu, Asn, Gln, 194 Lys, His, Ala, Tyr, Ile, Val or Gly; Xaa at position 47 is Ile, Gly, Val, Ser, Arg, Pro, or His; 195 196 Xaa at position 48 is Leu, Ser, Cys, Arg, Ile, His, Phe, Glu, 197 Lys, Thr, Ala, Met, Val or Asn; 198 Xaa at position 49 is Met, Arg, Ala, Gly, Pro, Asn, His, or 199 Asp; 200 Xaa at position 50 is Glu, Leu, Thr, Asp, Tyr, Lys, Asn, Ser, 201 Ala, Ile, Val, His, Phe, Met or Gln; 202 Xaa at position 51 is Asn, Arg, Met, Pro, Ser, Thr, or His; Xaa at position 52 is Asn, His, Arg, Leu, Gly, Ser, or Thr; 203 204 Xaa at position 53 is Leu, Thr, Ala, Gly, Glu, Pro, Lys, Ser, 205 or Met; 206 Xaa at position 54 is Arg, Asp, Ile, Ser, Val, Thr, Gln, Asn, 207 Lys, His, Ala or Leu; 208 Xaa at position 55 is Arg, Thr, Val, Ser, Leu, or Gly; 209 Xaa at position 56 is Pro, Gly, Cys, Ser, Gln, Glu, Arq, His, 210 Thr, Ala, Tyr, Phe, Leu, Val or Lys; 211 Xaa at position 57 is Asn or Gly; 212 Xaa at position 58 is Leu, Ser, Asp, Arg, Gln, Val, or Cys; 213 Xaa at position 59 is Glu Tyr, His, Leu, Pro, or Arg; 214 Xaa at position 60 is Ala, Ser, Pro, Tyr, Asn, or Thr; 215 Xaa at position 61 is Phe, Asn, Glu, Pro, Lys, Arg, or Ser; 216 Xaa at position 62 is Asn, His, Val, Arg, Pro, Thr, Asp, or 217 Ile; 218 Xaa at position 63 is Arg, Tyr, Trp, Lys, Ser, His, Pro, or 219 Val; 220 Xaa at position 64 is Ala, Asn, Pro, Ser, or Lys; 221 Xaa at position 65 is Val, Thr, Pro, His, Leu, Phe, or Ser; 222 Xaa at position 66 is Lys, Ile, Arg, Val, Asn, Glu, or Ser; 223 Xaa at position 67 is Ser, Ala, Phe, Val, Gly, Asn, Ile, Pro, 224 or His;

Xaa at position 68 is Leu, Val, Trp, Ser, Ile, Phe, Thr, or

225226

His;

- 227 Xaa at position 69 is Gln, Ala, Pro, Thr, Glu, Arg, Trp, Gly,
- 228 or Leu;
- 229 Xaa at position 70 is Asn, Leu, Val, Trp, Pro, or Ala;
- 230 Xaa at position 71 is Ala, Met, Leu, Pro, Arg, Glu, Thr, Gln,
- 231 Trp, or Asn;
- 232 Xaa at position 72 is Ser, Glu, Met, Ala, His, Asn, Arg, or
- 233 Asp
- 234 Xaa at position 73 is Ala, Glu, Asp, Leu, Ser, Gly, Thr, or
- 235 Arg;
- 236 Xaa at position 74 is Ile, Met, Thr, Pro, Arg, Gly, Ala;
- 237 Xaa at position 75 is Glu, Lys, Gly, Asp, Pro, Trp, Arg, Ser,
- 238 Gln, or Leu;
- 239 Xaa at position 76 is Ser, Val, Ala, Asn, Trp, Glu, Pro, Gly,
- 240 or Asp;
- 241 Xaa at position 77 is Ile, Ser, Arg, Thr, or Leu;
- 242 Xaa at position 78 is Leu, Ala, Ser, Glu, Phe, Gly, or Arg;
- 243 Xaa at position 79 is Lys, Thr, Asn, Met, Arg, Ile, Gly, or
- 244 Asp;
- 245 Xaa at position 80 is Asn, Trp, Val, Gly, Thr, Leu, Glu, or
- 246 Arg;
- 247 Xaa at position 81 is Leu, Gln, Gly, Ala, Trp, Arg, Val, or
- 248 Lys;
- 249 Xaa at position 82 is Leu, Gln, Lys, Trp, Arg, Asp, Glu, Asn,
- 250 His, Thr, Ser, Ala, Tyr, Phe, Ile, Met or Val;
- 251 Xaa at position 83 is Pro, Ala, Thr, Trp, Arg, or Met;
- 252 Xaa at position 84 is Cys, Glu, Gly, Arg, Met, or Val;
- 253 Xaa at position 85 is Leu, Asn, Val, or Gln;
- 254 Xaa at position 86 is Pro, Cys, Arg, Ala, or Lys;
- 255 Xaa at position 87 is Leu, Ser, Trp, or Gly;
- 256 Xaa at position 88 is Ala, Lys, Arg, Val, or Trp;
- 257 Xaa at position 89 is Thr, Asp, Cys, Leu, Val, Glu, His, Asn,
- 258 or Ser;
- 259 Xaa at position 90 is Ala, Pro, Ser, Thr, Gly, Asp, Ile, or
- 260 Met;
- 261 Xaa at position 91 is Ala, Pro, Ser, Thr, Phe, Leu, Asp, or
- 262 His;

- 263 Xaa at position 92 is Pro, Phe, Arg, Ser, Lys, His, Ala, Gly,
- 264 Ile or Leu;
- 265 Xaa at position 93 is Thr, Asp, Ser, Asn, Pro, Ala, Leu, or
- 266 Arg;
- 267 Xaa at position 94 is Arg, Ile, Ser, Glu, Leu, Val, Gln, Lys,
- 268 His, Ala, or Pro;
- 269 Xaa at position 95 is His, Gln, Pro, Arg, Val, Leu, Gly, Thr,
- 270 Asn, Lys, Ser, Ala, Trp, Phe, Ile, or Tyr;
- 271 Xaa at position 96 is Pro, Lys, Tyr, Gly, Ile, or Thr;
- 272 Xaa at position 97 is Ile, Val, Lys, Ala, or Asn;
- 273 Xaa at position 98 is His, Ile, Asn, Leu, Asp, Ala, Thr,
- Glu, Gln, Ser, Phe, Met, Val, Lys, Arg, Tyr or Pro;
- 275 Xaa at position 99 is Ile, Leu, Arg, Asp, Val, Pro, Gln,
- 276 Gly, Ser, Phe, or His;
- 277 Xaa at position 100 is Lys, Tyr, Leu, His, Arg, Ile, Ser, Gln,
- 278 or Pro;
- 279 Xaa at position 101 is Asp, Pro, Met, Lys, His, Thr, Val,
- Tyr, Glu, Asn, Ser, Ala, Gly, Ile, Leu, or Gln;
- 281 Xaa at position 102 is Gly, Leu, Glu, Lys, Ser, Tyr, or Pro;
- 282 Xaa at position 103 is Asp, or Ser;
- 283 Xaa at position 104 is Trp, Val, Cys, Tyr, Thr, Met, Pro, Leu,
- 284 Gln, Lys, Ala, Phe, or Gly;
- 285 Xaa at position 105 is Asn, Pro, Ala, Phe, Ser, Trp, Gln, Tyr,
- Leu, Lys, Ile, Asp, or His;
- 287 Xaa at position 106 is Glu, Ser, Ala, Lys, Thr, Ile, Gly, or
- 288 Pro;
- 289 Xaa at position 108 is Arg, Lys, Asp, Leu, Thr, Ile, Gln, His,
- 290 Ser, Ala or Pro;
- 291 Xaa at position 109 is Arg, Thr, Pro, Glu, Tyr, Leu, Ser, or
- 292 Gly;
- 293 Xaa at position 110 is Lys, Ala, Asn, Thr, Leu, Arg, Gln, His,
- 294 Glu, Ser, or Trp;
- 295 Xaa at position 111 is Leu, Ile, Arg, Asp, or Met;
- 296 Xaa at position 112 is Thr, Val, Gln, Tyr, Glu, His, Ser, or
- 297 Phe;
- 298 Xaa at position 113 is Phe, Ser, Cys, His, Gly, Trp, Tyr, Asp,

299 Lys, Leu, Ile, Val or Asn; Xaa at position 114 is Tyr, Cys, His, Ser, Trp, Arg, or Leu; 300 301 Xaa at position 115 is Leu, Asn, Val, Pro, Arg, Ala, His, Thr, 302 Trp, or Met; 303 Xaa at position 116 is Lys, Leu, Pro, Thr, Met, Asp, Val, Glu, 304 Arg, Trp, Ser, Asn, His, Ala, Tyr, Phe, Gln, or Ile; Xaa at position 117 is Thr, Ser, Asn, Ile, Trp, Lys, or Pro; 305 306 Xaa at position 118 is Leu, Ser, Pro, Ala, Glu, Cys, Asp, or 307 Tyr; 308 Xaa at position 119 is Glu, Ser, Lys, Pro, Leu, Thr, Tyr, or 309 310 Xaa at position 120 is Asn, Ala, Pro, Leu, His, Val, or Gln; 311 Xaa at position 121 is Ala, Ser, Ile, Asn, Pro, Lys, Asp, or 312 Gly; 313 Xaa at position 122 is Gln, Ser, Met, Trp, Arg, Phe, Pro, His, 314 Ile, Tyr, or Cys; 315 Xaa at position 123 is Ala, Met, Glu, His, Ser, Pro, Tyr, or 316 Leu. 317 318 wherein from 1 to 14 amino acids can optionally be deleted 319 from the N-terminus and/or from 1 to 15 amino acids can 320 optionally be deleted from the C-terminus of said modified 321 human interleukin-3 amino acid sequence; and wherein from 0 to 322 44 of the amino acids designated by Xaa are different from the 323 corresponding amino acids of native (1-133) human interleukin-324 3 and

328329

327

325326

26-27	49-50	83-84
27-28	50-51	84-85
28-29	51-52	85-86
29-30	52-53	86-87
30-31	53-54	87-88
31-32	54-55	88-89

wherein the N-terminus is joined to the C-terminus directly or

through a linker (L2) capable of joining the N-terminus to the

C-terminus and having new C- and N-termini at amino acids:

32-33	64-65	89-90
33-34	65-66	90-91
34-35	66-67	91-92
35-36	67-68	92-93
36-37	68-69	97-98
37-38	69-70	98-99
38-39	70-71	99-100
39-40	71-72	100-101
40-41	72-73	101-102
41-42	82-83	102-103
		or 103-104
		respectively;

wherein L1 is a linker capable of linking R1 to R2 and

said hematopoietic protein can optionally be immediately preceded by (methionine $^{-1}$ ), (alanine $^{-1}$ ) or (methionine $^{-2}$ , alanine $^{-1}$ ).

1 2

8. A hematopoietic protein comprising; an amino acid sequence of the formula:

$$R_1-L_1-R_2$$
,  $R_2-L_1-R_1$ ,  $R_1-R_2$ , or  $R_2-R_1$ 

wherein  $R_1$  is a polypeptide comprising; a modified human G-CSF amino acid sequence of the formula:

1 10 Xaa Xaa Xaa Gly Pro Ala Ser Ser Leu Pro Gln Ser Xaa

Leu Leu Xaa Xaa Xaa Glu Gln Val Xaa Lys Xaa Gln Gly Xaa Gly

30 40

 Ala Xaa Leu Gln Glu Xaa Leu Xaa Ala Thr Tyr Lys Leu Xaa Xaa

Xaa Glu Xaa Xaa Val Xaa Xaa Gly His Ser Xaa Gly Ile Pro Trp 20

22 Ala Pro Leu Ser Ser Xaa Pro Ser Xaa Ala Leu Xaa Leu Ala Gly

```
23
24
                             80
25
    Xaa Leu Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu
26
27
                                                  100
    Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu
28
29
30
                             110
31
    Xaa Thr Leu Gln Xaa Asp Val Ala Asp Phe Ala Xaa Thr Ile Trp
32
33
        120
34
    Gln Gln Met Glu Xaa Xaa Gly Met Ala Pro Ala Leu Gln Pro Thr
35
36
                             140
37
    Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Xaa Gln Xaa Xaa Ala
38
39
        150
                                                  160
40
    Gly Gly Val Leu Val Ala Ser Xaa Leu Gln Xaa Phe Leu Xaa Xaa
41
42
                             170
43
    Ser Tyr Arg Val Leu Xaa Xaa Leu Ala Gln Pro (SEQ ID NO:1)
44
45
    wherein
46
47
    Xaa at position 1 is Thr, Ser, Arg, Tyr or Gly;
48
    Xaa at position 2 is Pro or Leu;
49
    Xaa at position 3 is Leu, Arg, Tyr or Ser;
50
    Xaa at position 13 is Phe, Ser, His, Thr or Pro;
51
    Xaa at position 16 is Lys, Pro, Ser, Thr or His;
52
    Xaa at position 17 is Cys, Ser, Gly, Ala, Ile, Tyr or
53
         Arg;
54
    Xaa at position 18 is Leu, Thr, Pro, His, Ile or Cys;
55
    Xaa at position 22 is Arg, Tyr, Ser, Thr or Ala;
56
    Xaa at position 24 is Ile, Pro, Tyr or Leu;
57
    Xaa at position 27 is Asp, or Gly;
58
    Xaa at position 30 is Ala, Ile, Leu or Gly;
59
    Xaa at position 34 is Lys or Ser;
60
    Xaa at position 36 is Cys or Ser;
61
    Xaa at position 42 is Cys or Ser;
62
    Xaa at position 43 is His, Thr, Gly, Val, Lys, Trp, Ala,
63
         Arg, Cys, or Leu;
64
    Xaa at position 44 is Pro, Gly, Arg, Asp, Val, Ala, His,
65
         Trp, Gln, or Thr;
66
    Xaa at position 46 is Glu, Arg, Phe, Arg, Ile or Ala;
67
    Xaa at position 47 is Leu or Thr;
68
    Xaa at position 49 is Leu, Phe, Arg or Ser;
69
    Xaa at position 50 is Leu, Ile, His, Pro or Tyr;
```

```
70
     Xaa at position 54 is Leu or His;
71
     Xaa at position 64 is Cys or Ser;
72
     Xaa at position 67 is Gln, Lys, Leu or Cys;
73
     Xaa at position 70 is Gln, Pro, Leu, Arg or Ser;
74
     Xaa at position 74 is Cys or Ser;
75
     Xaa at position 104 is Asp, Gly or Val;
76
     Xaa at position 108 is Leu, Ala, Val, Arg, Trp, Gln or
77
          Gly;
78
     Xaa at position 115 is Thr, His, Leu or Ala;
79
     Xaa at position 120 is Gln, Gly, Arg, Lys or His
80
     Xaa at position 123 is Glu, Arg, Phe or Thr
81
     Xaa at position 144 is Phe, His, Arg, Pro, Leu, Gln or
82
          Glu:
83
     Xaa at position 146 is Arg or Gln;
84
     Xaa at position 147 is Arg or Gln;
85
     Xaa at position 156 is His, Gly or Ser;
     Xaa at position 159 is Ser, Arg, Thr, Tyr, Val or Gly;
86
87
     Xaa at position 162 is Glu, Leu, Gly or Trp;
     Xaa at position 163 is Val, Gly, Arg or Ala;
88
89
     Xaa at position 169 is Arg, Ser, Leu, Arg or Cys;
90
     Xaa at position 170 is His, Arg or Ser;
91
92
     wherein optionally 1-11 amino acids from the N-terminus and 1-
93
     5 from the C-terminus can be deleted from said modified human
94
     G-CSF amino acid sequence and
95
96
     wherein the N-terminus is joined to the C-terminus directly or
97
     through a linker capable of joining the N-terminus to the C-
98
     terminus and having new C- and N-termini at amino acids:
99
100
101
     38-39
                             62-63
                                                 123-124
102
     39-40
                             63-64
                                                 124-125
103
     40 - 41
                             64 - 65
                                                 125-126
104
     41 - 42
                             65-66
                                                 126-127
105
     42 - 43
                             66-67
                                                 128-129
106
     43 - 44
                             67-68
                                                 128-129
107
     45 - 46
                             68-69
                                                 129-130
108
     48 - 49
                             69-70
                                                 130-131
109
     49-50
                             70-71
                                                 131-132
110
     52-53
                                                 132-133
                             71-72
111
     53-54
                             91 - 92
                                                 133-134
112
     54-55
                             92 - 93
                                                 134-135
113
     55-56
                             93 - 94
                                                 135-136
114
     56-57
                             94-95
                                                 136-137
115
     57-58
                             95-96
                                                 137-138
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116
   58-59
                  96-97
                               138-139
                  97-98
117
   59-60
                               139-140
118
   60-61
                  98-99
                               140-141
119
   61-62
                  99-100
                               141-142
120
                               or 142-143
121
                               respectively; and
122
123
      R2 is a polypeptide comprising a modified human IL-3
124
   amino acid sequence of the formula:
125
126
   Ala Pro Met Thr Gln Thr Thr Ser Leu Lys Thr Ser Trp Val Asn
127
              5
                           10
                                         15
128
129
   130
              20
                           25
                                         30
131
132
   Xaa Xaa Xaa Xaa Xaa Xaa Xaa Asn Xaa Xaa Xaa Xaa Xaa
133
              35
                           40
                                         45
134
135
   136
              50
                           55
                                         60
137
138
   139
                           70
              65
                                         75
140
141
   142
              80
                           8.5
                                         90
143
144
   145
              95
                           100
                                         105
146
147
   148
              110
                           115
                                         120
149
150
   Xaa Xaa Xaa Gln Gln Thr Thr Leu Ser Leu Ala Ile Phe
151
              125
                           130 (SEQ ID NO:2)
152
```

153 wherein Xaa at position 17 is Ser, Lys, Gly, Asp, Met, Gln, or 154 155 Xaa at position 18 is Asn, His, Leu, Ile, Phe, Arg, or Gln; 156 Xaa at position 19 is Met, Phe, Ile, Arg, Gly, Ala, or Cys; 157 Xaa at position 20 is Ile, Cys, Gln, Glu, Arg, Pro, or Ala; 158 Xaa at position 21 is Asp, Phe, Lys, Arg, Ala, Gly, Glu, Gln, 159 Asn, Thr, Ser or Val; Xaa at position 22 is Glu, Trp, Pro, Ser, Ala, His, Asp, Asn, 160 161 Gln, Leu, Val or Gly; 162 Xaa at position 23 is Ile, Val, Ala, Gly, Trp, Lys, Phe, 163 Leu, Ser, or Arg; 164 Xaa at position 24 is Ile, Gly, Val, Arg, Ser, Phe, or Leu; Xaa at position 25 is Thr, His, Gly, Gln, Arg, Pro, or Ala; 165 166 Xaa at position 26 is His, Thr, Phe, Gly, Arg, Ala, or Trp; 167 Xaa at position 27 is Leu, Gly, Arg, Thr, Ser, or Ala; 168 Xaa at position 28 is Lys, Arg, Leu, Gln, Gly, Pro, Val or 169 170 Xaa at position 29 is Gln, Asn, Leu, Pro, Arq, or Val; 171 Xaa at position 30 is Pro, His, Thr, Gly, Asp, Gln, Ser, Leu, 172 or Lys; Xaa at position 31 is Pro, Asp, Gly, Ala, Arg, Leu, or Gln; 173 174 Xaa at position 32 is Leu, Val, Arg, Gln, Asn, Gly, Ala, or 175 Glu; 176 Xaa at position 33 is Pro, Leu, Gln, Ala, Thr, or Glu; Xaa at position 34 is Leu, Val, Gly, Ser, Lys, Glu, Gln, Thr, 177 178 Arg, Ala, Phe, Ile or Met; 179 Xaa at position 35 is Leu, Ala, Gly, Asn, Pro, Gln, or Val; 180 Xaa at position 36 is Asp, Leu, or Val; 181 Xaa at position 37 is Phe, Ser, Pro, Trp, or Ile; 182 Xaa at position 38 is Asn, or Ala; 183 Xaa at position 40 is Leu, Trp, or Arg; 184 Xaa at position 41 is Asn, Cys, Arg, Leu, His, Met, or Pro; 185 Xaa at position 42 is Gly, Asp, Ser, Cys, Asn, Lys, Thr, Leu, 186 Val, Glu, Phe, Tyr, Ile, Met or Ala; Xaa at position 43 is Glu, Asn, Tyr, Leu, Phe, Asp, Ala, Cys, 187

Gln, Arg, Thr, Gly or Ser;

188

224

or His;

189 Xaa at position 44 is Asp, Ser, Leu, Arg, Lys, Thr, Met, Trp, 190 Glu, Asn, Gln, Ala or Pro; 191 Xaa at position 45 is Gln, Pro, Phe, Val, Met, Leu, Thr, Lys, 192 Trp, Asp, Asn, Arg, Ser, Ala, Ile, Glu or His; 193 Xaa at position 46 is Asp, Phe, Ser, Thr, Cys, Glu, Asn, Gln, 194 Lys, His, Ala, Tyr, Ile, Val or Gly; 195 Xaa at position 47 is Ile, Gly, Val, Ser, Arg, Pro, or His; 196 Xaa at position 48 is Leu, Ser, Cys, Arg, Ile, His, Phe, Glu, Lys, Thr, Ala, Met, Val or Asn; 197 198 Xaa at position 49 is Met, Arg, Ala, Gly, Pro, Asn, His, or 199 Asp; 200 Xaa at position 50 is Glu, Leu, Thr, Asp, Tyr, Lys, Asn, Ser, 201 Ala, Ile, Val, His, Phe, Met or Gln; 202 Xaa at position 51 is Asn, Arg, Met, Pro, Ser, Thr, or His; 203 Xaa at position 52 is Asn, His, Arg, Leu, Gly, Ser, or Thr; 204 Xaa at position 53 is Leu, Thr, Ala, Gly, Glu, Pro, Lys, Ser, 205 or Met; 206 Xaa at position 54 is Arg, Asp, Ile, Ser, Val, Thr, Gln, Asn, 207 Lys, His, Ala or Leu; 208 Xaa at position 55 is Arg, Thr, Val, Ser, Leu, or Gly; Xaa at position 56 is Pro, Gly, Cys, Ser, Gln, Glu, Arg, His, 209 210 Thr, Ala, Tyr, Phe, Leu, Val or Lys; 211 Xaa at position 57 is Asn or Gly; 212 Xaa at position 58 is Leu, Ser, Asp, Arg, Gln, Val, or Cys; Xaa at position 59 is Glu Tyr, His, Leu, Pro, or Arg; 213 214 Xaa at position 60 is Ala, Ser, Pro, Tyr, Asn, or Thr; 215 Xaa at position 61 is Phe, Asn, Glu, Pro, Lys, Arg, or Ser; 216 Xaa at position 62 is Asn, His, Val, Arg, Pro, Thr, Asp, or 217 Ile; 218 Xaa at position 63 is Arg, Tyr, Trp, Lys, Ser, His, Pro, or 219 Val; 220 Xaa at position 64 is Ala, Asn, Pro, Ser, or Lys; 221 Xaa at position 65 is Val, Thr, Pro, His, Leu, Phe, or Ser; 222 Xaa at position 66 is Lys, Ile, Arg, Val, Asn, Glu, or Ser;

Xaa at position 67 is Ser, Ala, Phe, Val, Gly, Asn, Ile, Pro,

- 225 Xaa at position 68 is Leu, Val, Trp, Ser, Ile, Phe, Thr, or
- 226 His;
- 227 Xaa at position 69 is Gln, Ala, Pro, Thr, Glu, Arg, Trp, Gly,
- 228 or Leu;
- 229 Xaa at position 70 is Asn, Leu, Val, Trp, Pro, or Ala;
- 230 Xaa at position 71 is Ala, Met, Leu, Pro, Arg, Glu, Thr, Gln,
- 231 Trp, or Asn;
- 232 Xaa at position 72 is Ser, Glu, Met, Ala, His, Asn, Arg, or
- 233 Asp;
- 234 Xaa at position 73 is Ala, Glu, Asp, Leu, Ser, Gly, Thr, or
- 235 Arg;
- 236 Xaa at position 74 is Ile, Met, Thr, Pro, Arg, Gly, Ala;
- 237 Xaa at position 75 is Glu, Lys, Gly, Asp, Pro, Trp, Arg, Ser,
- 238 Gln, or Leu;
- 239 Xaa at position 76 is Ser, Val, Ala, Asn, Trp, Glu, Pro, Gly,
- 240 or Asp;
- 241 Xaa at position 77 is Ile, Ser, Arg, Thr, or Leu;
- 242 Xaa at position 78 is Leu, Ala, Ser, Glu, Phe, Gly, or Arg;
- 243 Xaa at position 79 is Lys, Thr, Asn, Met, Arg, Ile, Gly, or
- 244 Asp;
- 245 Xaa at position 80 is Asn, Trp, Val, Gly, Thr, Leu, Glu, or
- 246 Arg;
- 247 Xaa at position 81 is Leu, Gln, Gly, Ala, Trp, Arg, Val, or
- 248 Lys;
- 249 Xaa at position 82 is Leu, Gln, Lys, Trp, Arg, Asp, Glu, Asn,
- 250 His, Thr, Ser, Ala, Tyr, Phe, Ile, Met or Val;
- 251 Xaa at position 83 is Pro, Ala, Thr, Trp, Arg, or Met;
- 252 Xaa at position 84 is Cys, Glu, Gly, Arg, Met, or Val;
- 253 Xaa at position 85 is Leu, Asn, Val, or Gln;
- 254 Xaa at position 86 is Pro, Cys, Arg, Ala, or Lys;
- 255 Xaa at position 87 is Leu, Ser, Trp, or Gly;
- 256 Xaa at position 88 is Ala, Lys, Arg, Val, or Trp;
- 257 Xaa at position 89 is Thr, Asp, Cys, Leu, Val, Glu, His, Asn,
- 258 or Ser;
- 259 Xaa at position 90 is Ala, Pro, Ser, Thr, Gly, Asp, Ile, or
- 260 Met;

261 Xaa at position 91 is Ala, Pro, Ser, Thr, Phe, Leu, Asp, or 262 His; 263 Xaa at position 92 is Pro, Phe, Arg, Ser, Lys, His, Ala, Gly, 264 Ile or Leu; Xaa at position 93 is Thr, Asp, Ser, Asn, Pro, Ala, Leu, or 265 266 267 Xaa at position 94 is Arg, Ile, Ser, Glu, Leu, Val, Gln, Lys, 268 His, 269 Ala, or Pro; 270 Xaa at position 95 is His, Gln, Pro, Arg, Val, Leu, Gly, Thr, 271 Asn, 272 Lys, Ser, Ala, Trp, Phe, Ile, or Tyr; Xaa at position 96 is Pro, Lys, Tyr, Gly, Ile, or Thr; 273 274 Xaa at position 97 is Ile, Val, Lys, Ala, or Asn; 275 Xaa at position 98 is His, Ile, Asn, Leu, Asp, Ala, Thr, 276 Glu, Gln, Ser, Phe, Met, Val, Lys, Arg, Tyr or Pro; 277 Xaa at position 99 is Ile, Leu, Arg, Asp, Val, Pro, Gln, 278 Gly, Ser, Phe, or His; 279 Xaa at position 100 is Lys, Tyr, Leu, His, Arg, Ile, Ser, Gln, 280 or Pro; 281 Xaa at position 101 is Asp, Pro, Met, Lys, His, Thr, Val, 282 Tyr, Glu, Asn, Ser, Ala, Gly, Ile, Leu, or Gln; 283 Xaa at position 102 is Gly, Leu, Glu, Lys, Ser, Tyr, or Pro; 284 Xaa at position 103 is Asp, or Ser; 285 Xaa at position 104 is Trp, Val, Cys, Tyr, Thr, Met, Pro, Leu, 286 Gln, Lys, Ala, Phe, or Gly; 287 Xaa at position 105 is Asn, Pro, Ala, Phe, Ser, Trp, Gln, Tyr, 288 Leu, Lys, Ile, Asp, or His; 289 Xaa at position 106 is Glu, Ser, Ala, Lys, Thr, Ile, Gly, or 290 Pro; 291 Xaa at position 108 is Arg, Lys, Asp, Leu, Thr, Ile, Gln, His, 292 Ser, Ala or Pro; 293 Xaa at position 109 is Arg, Thr, Pro, Glu, Tyr, Leu, Ser, or 294 Gly;

Xaa at position 110 is Lys, Ala, Asn, Thr, Leu, Arg, Gln, His,

295296

Glu, Ser, or Trp;

297 Xaa at position 111 is Leu, Ile, Arg, Asp, or Met; 298 Xaa at position 112 is Thr, Val, Gln, Tyr, Glu, His, Ser, or 299 Phe: 300 Xaa at position 113 is Phe, Ser, Cys, His, Gly, Trp, Tyr, Asp, 301 Lys, Leu, Ile, Val or Asn; 302 Xaa at position 114 is Tyr, Cys, His, Ser, Trp, Arg, or Leu; 303 Xaa at position 115 is Leu, Asn, Val, Pro, Arg, Ala, His, Thr, 304 Trp, or Met; 305 Xaa at position 116 is Lys, Leu, Pro, Thr, Met, Asp, Val, Glu, 306 Arg, Trp, Ser, Asn, His, Ala, Tyr, Phe, Gln, or Ile; 307 Xaa at position 117 is Thr, Ser, Asn, Ile, Trp, Lys, or Pro; 308 Xaa at position 118 is Leu, Ser, Pro, Ala, Glu, Cys, Asp, or 309 Tyr; 310 Xaa at position 119 is Glu, Ser, Lys, Pro, Leu, Thr, Tyr, or 311 Arq; 312 Xaa at position 120 is Asn, Ala, Pro, Leu, His, Val, or Gln; Xaa at position 121 is Ala, Ser, Ile, Asn, Pro, Lys, Asp, or 313 314 Gly; Xaa at position 122 is Gln, Ser, Met, Trp, Arg, Phe, Pro, His, 315 316 Ile, Tyr, or Cys; 317 Xaa at position 123 is Ala, Met, Glu, His, Ser, Pro, Tyr, or 318 Leu, 319 320 wherein from 1 to 14 amino acids can optionally be deleted 321 from the N-terminus and/or from 1 to 15 amino acids can 322 optionally be deleted from the C-terminus; and wherein from 1 323 to 44 of the amino acids designated by Xaa are different from 324 the corresponding amino acids of native (1-133) human 325 interleukin-3 and 326 327 L<sub>1</sub> is a linker capable of linking R<sub>1</sub> to R<sub>2</sub> and 328 329 additionally said hematopoietic protein can be immediately preceded by  $(methionine^{-1})$ ,  $(alanine^{-1})$  or 330 (methionine $^{-2}$ , alanine $^{-1}$ ). 331

```
1
               A hematopoietic protein comprising an amino acid sequence
2
    of the formula:
3
4
               R_1-L_1-R_2, R_2-L_1-R_1, R_1-R_2, or R_2-R_1
5
6
         wherein R<sub>1</sub> is a polypeptide comprising; a modified human
7
    G-CSF amino acid sequence of the formula:
8
9
                                           10
10
    Xaa Xaa Xaa Gly Pro Ala Ser Ser Leu Pro Gln Ser Xaa
11
12
                              20
13
    Leu Leu Xaa Xaa Glu Gln Val Xaa Lys Xaa Gln Gly Xaa Gly
14
15
        30
    Ala Xaa Leu Gln Glu Xaa Leu Xaa Ala Thr Tyr Lys Leu Xaa Xaa
16
17
18
                              50
19
    Xaa Glu Xaa Xaa Val Xaa Xaa Gly His Ser Xaa Gly Ile Pro Trp
20
21
        60
                                                   70
22
    Ala Pro Leu Ser Ser Xaa Pro Ser Xaa Ala Leu Xaa Leu Ala Gly
23
24
                              80
25
    Xaa Leu Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu
26
27
28
    Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu
29
30
31
    Xaa Thr Leu Gln Xaa Asp Val Ala Asp Phe Ala Xaa Thr Ile Trp
32
33
        120
                                                   130
34
    Gln Gln Met Glu Xaa Xaa Gly Met Ala Pro Ala Leu Gln Pro Thr
35
36
                              140
37
    Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Xaa Gln Xaa Xaa Ala
38
39
        150
                                                   160
40
    Gly Gly Val Leu Val Ala Ser Xaa Leu Gln Xaa Phe Leu Xaa Xaa
41
42
                              170
43
    Ser Tyr Arg Val Leu Xaa Xaa Leu Ala Gln Pro (SEQ ID NO:1)
44
45
    wherein
```

```
46
47
    Xaa at position 1 is Thr, Ser, Arg, Tyr or Gly;
48
    Xaa at position 2 is Pro or Leu;
49
    Xaa at position 3 is Leu, Arg, Tyr or Ser;
50
    Xaa at position 13 is Phe, Ser, His, Thr or Pro;
51
    Xaa at position 16 is Lys, Pro, Ser, Thr or His;
52
    Xaa at position 17 is Cys, Ser, Gly, Ala, Ile, Tyr or
53
         Arq;
54
    Xaa at position 18 is Leu, Thr, Pro, His, Ile or Cys;
55
    Xaa at position 22 is Arg, Tyr, Ser, Thr or Ala;
    Xaa at position 24 is Ile, Pro, Tyr or Leu;
56
57
    Xaa at position 27 is Asp, or Gly;
58
    Xaa at position 30 is Ala, Ile, Leu or Gly;
59
    Xaa at position 34 is Lys or Ser;
60
    Xaa at position 36 is Cys or Ser;
61
    Xaa at position 42 is Cys or Ser;
62
    Xaa at position 43 is His, Thr, Gly, Val, Lys, Trp, Ala,
63
         Arg, Cys, or Leu;
64
    Xaa at position 44 is Pro, Gly, Arg, Asp, Val, Ala, His,
65
         Trp, Gln, or Thr;
66
    Xaa at position 46 is Glu, Arg, Phe, Arg, Ile or Ala;
67
    Xaa at position 47 is Leu or Thr;
68
    Xaa at position 49 is Leu, Phe, Arg or Ser;
69
    Xaa at position 50 is Leu, Ile, His, Pro or Tyr;
70
    Xaa at position 54 is Leu or His;
71
    Xaa at position 64 is Cys or Ser;
72
    Xaa at position 67 is Gln, Lys, Leu or Cys;
73
    Xaa at position 70 is Gln, Pro, Leu, Arg or Ser;
74
    Xaa at position 74 is Cys or Ser;
75
    Xaa at position 104 is Asp, Gly or Val;
    Xaa at position 108 is Leu, Ala, Val, Arg, Trp, Gln or
76
77
         Glv;
78
    Xaa at position 115 is Thr, His, Leu or Ala;
    Xaa at position 120 is Gln, Gly, Arg, Lys or His
79
80
    Xaa at position 123 is Glu, Arg, Phe or Thr
81
    Xaa at position 144 is Phe, His, Arg, Pro, Leu, Gln or
82
         Glu;
83
    Xaa at position 146 is Arg or Gln;
84
    Xaa at position 147 is Arg or Gln;
85
    Xaa at position 156 is His, Gly or Ser;
86
    Xaa at position 159 is Ser, Arg, Thr, Tyr, Val or Gly;
87
    Xaa at position 162 is Glu, Leu, Gly or Trp;
    Xaa at position 163 is Val, Gly, Arg or Ala;
88
89
    Xaa at position 169 is Arg, Ser, Leu, Arg or Cys;
90
    Xaa at position 170 is His, Arg or Ser,
91
```

```
92
    wherein optionally 1-11 amino acids from the N-terminus and 1-
93
     5 from the C-terminus can be deleted from said modified human
94
    G-CSF amino acid sequence and
95
96
    wherein the N-terminus is joined to the C-terminus directly or
97
     through a linker capable of joining the N-terminus to the C-
98
     terminus and having new C- and N-termini at amino acids:
99
100
101
     38-39
                            62-63
                                               123-124
102
     39-40
                            63-64
                                               124-125
103
     40-41
                            64-65
                                               125-126
104
     41-42
                            65-66
                                               126-127
105
    42-43
                            66-67
                                               128-129
106
     43-44
                            67-68
                                               128-129
107
     45-46
                            68-69
                                               129-130
108
    48-49
                            69-70
                                               130-131
109
     49-50
                            70-71
                                               131-132
     52-53
110
                            71-72
                                               132-133
111
     53-54
                            91-92
                                               133-134
112
     54-55
                            92-93
                                               134-135
113
     55-56
                            93-94
                                               135-136
114
     56-57
                            94 - 95
                                               136-137
115
     57-58
                            95-96
                                               137-138
116
     58-59
                            96-97
                                               138-139
117
     59-60
                            97-98
                                               139-140
118
     60-61
                            98-99
                                               140-141
119
     61-62
                            99-100
                                               141-142
120
                                               or 142-143
121
                                               respectively; and
122
123
          R2 is a polypeptide comprising a modified human c-mpl
124
     ligand amino acid sequence of the formula:
125
126
     SerProAlaProProAlaCysAspLeuArgValLeuSerLysLeuLeuArgAspSer
127
128
129
    HisValLeuHisSerArgLeuSerGlnCysProGluValHisProLeuProThrPro
130
                    25
                                   30
131
    132
133
        40
                       45
                                      50
                                                      55
134
135
    ThrLysAlaGlnAspIleLeuGlyAlaValThrLeuLeuGluGlyValMetAla
```

75

65

136

```
137
     AlaArgGlyGlnLeuGlyProThrCysLeuSerSerLeuLeuGlyGlnLeuSerGly
138
139
                              85
                                              90
140
141
     GlnValArgLeuLeuGlyAlaLeuGlnSerLeuLeuGlyThrGlnXaaXaaXaa
142
                                 105
143
144
     XaaGlyArgThrThrAlaHisLysAspProAsnAlaIlePheLeuSerPheGlnHis
145
     115
                     120
                                    125
146
147
     LeuLeuArgGlyLysValArgPheLeuMetLeuValGlyGlySerThrLeuCysVal
148
        135
                                       145
                                                       150
149
150
     Arg (SEQ ID NO:256)
151
152
     wherein
153
154
     Xaa at position 112 is deleted or Leu, Ala, Val, Ile, Pro,
155
     Phe, Trp, or Met;
156
     Xaa at position 113 is deleted or Pro, Phe, Ala, Val,
                                                              Leu,
157
     Ile, Trp, or Met;
158
     Xaa at position 114 is deleted or Pro, Phe, Ala, Val,
                                                              Leu,
159
     Ile, Trp, or Met;
160
     Xaa at position 115 is deleted or Gln, Gly, Ser, Thr,
                                                               Tyr, or
161
     Asn, and
162
163
     wherein the N-terminus is joined to the C-terminus directly or
164
     through a linker (L2) capable of joining the N-terminus to the
165
     C-terminus and having new C- and N-termini at amino acids:
166
```

26-27	51-52	108-109
27-28	52-53	109-110
28-29	53-54	110-111
29-30	54-55	111-112
30-31	55-56	112-113
32-33	56-57	113-114
33-34	57-58	114-115
34-35	58-59	115-116
36-37	59-60	116-117
37-38	78-79	117-118
38-39	79-80	118-119

40-41	80-81	119-120
41-42	81-82	120-121
42-43	82-83	121-122
43-44	83-84	122-123
44-45	84-85	123-124
46-47	85-86	124-125
47-48	86-87	125-126
48-49	87-88	126-127
50-51	88-89	or 127-128;

wherein L1 is a linker capable of linking R1 to R2 and

additionally said hematopoietic protein can be immediately preceded by (methionine $^{-1}$ ), (alanine $^{-1}$ ) or (methionine $^{-2}$ , alanine $^{-1}$ ).

5

$$R_1-L_1-R_2$$
,  $R_2-L_1-R_1$ ,  $R_1-R_2$ , or  $R_2-R_1$ 

 wherein  $R_1$  is a polypeptide comprising a modified human c-mpl ligand amino acid sequence of the formula:

 $\begin{tabular}{ll} SerProAlaProProAlaCysAspLeuArgValLeuSerLysLeuLeuArgAspSer \\ 1 & 5 & 10 & 15 \end{tabular}$ 

HisValLeuHisSerArgLeuSerGlnCysProGluValHisProLeuProThrPro 20 25 30 35

ValLeuLeuProAlaValAspPheSerLeuGlyGluTrpLysThrGlnMetGluGlu 40 45 50 55

ThrLysAlaGlnAspIleLeuGlyAlaValThrLeuLeuLeuGluGlyValMetAla
60 65 70 75

AlaArgGlyGlnLeuGlyProThrCysLeuSerSerLeuLeuGlyGlnLeuSerGly
80 85 90 95

GlnValArgLeuLeuGlyAlaLeuGlnSerLeuLeuGlyThrGlnXaaXaaXaa 100 105 110

 ${\tt XaaGlyArgThrThrAlaHisLysAspProAsnAlaIlePheLeuSerPheGlnHis}$ 

```
28
                   120
    115
                                   125
                                                  130
29
30
    LeuLeuArgGlyLysValArgPheLeuMetLeuValGlyGlySerThrLeuCysVal
31
                      140
                                      145
32
33
    Arg (SEQ ID NO:256)
34
    153
35
36
    wherein
37
38
    Xaa at position 112 is deleted or Leu, Ala, Val, Ile, Pro,
39
    Phe, Trp, or Met;
40
    Xaa at position 113 is deleted or Pro, Phe, Ala, Val,
                                                             Leu,
41
    Ile, Trp, or Met;
42
    Xaa at position 114 is deleted or Pro, Phe, Ala, Val,
43
    Ile, Trp, or Met;
44
    Xaa at position 115 is deleted or Gln, Gly, Ser, Thr,
                                                             Tyr, or
45
    Asn, and
46
47
    wherein the N-terminus is joined to the C-terminus directly or
48
    through a linker (L2) capable of joining the N-terminus to the
```

0.6.07	T51 50	1100 100
26-27	51-52	108-109
27-28	52-53	109-110
28-29	53-54	110-111
29-30	54-55	111-112
30-31	55-56	112-113
32-33	56-57	113-114
33-34	57-58	114-115
34-35	58-59	115-116
36-37	59-60	116-117
37-38	78-79	117-118
38-39	79-80	118-119
40-41	80-81	119-120
41-42	81-82	120-121
42-43	82-83	121-122
43-44	83-84	122-123
44-45	84-85	123-124
46-47	85-86	124-125
47-48	86-87	125-126

C-terminus and having new C- and N-termini at amino acids:

48-49	87-88	126-127
50-51	88-89	or 127-128;

wherein R2 is a polypeptide comprising a modified human IL-3 amino acid sequence of the formula: Ala Pro Met Thr Gln Thr Thr Ser Leu Lys Thr Ser Trp Val Asn Xaa Xaa Xaa Xaa Xaa Xaa Xaa Asn Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Gln Gln Thr Thr Leu Ser Leu Ala Ile Phe 130 (SEO ID NO:2) wherein Xaa at position 17 is Ser, Lys, Gly, Asp, Met, Gln, or 

Xaa at position 18 is Asn, His, Leu, Ile, Phe, Arg, or Gln;

120

85 Xaa at position 19 is Met, Phe, Ile, Arg, Gly, Ala, or Cys; 86 Xaa at position 20 is Ile, Cys, Gln, Glu, Arg, Pro, or Ala; 87 Xaa at position 21 is Asp, Phe, Lys, Arg, Ala, Gly, Glu, Gln, 88 Asn, Thr, Ser or Val; 89 Xaa at position 22 is Glu, Trp, Pro, Ser, Ala, His, Asp, Asn, 90 Gln, Leu, Val or Gly; Xaa at position 23 is Ile, Val, Ala, Gly, Trp, Lys, Phe, 91 92 Leu, Ser, or Arg; 93 Xaa at position 24 is Ile, Gly, Val, Arg, Ser, Phe, or Leu; 94 Xaa at position 25 is Thr, His, Gly, Gln, Arg, Pro, or Ala; 95 Xaa at position 26 is His, Thr, Phe, Gly, Arg, Ala, or Trp; Xaa at position 27 is Leu, Gly, Arg, Thr, Ser, or Ala; 96 97 Xaa at position 28 is Lys, Arg, Leu, Gln, Gly, Pro, Val or 98 Trp; 99 Xaa at position 29 is Gln, Asn, Leu, Pro, Arg, or Val; 100 Xaa at position 30 is Pro, His, Thr, Gly, Asp, Gln, Ser, Leu, 101 or Lys; 102 Xaa at position 31 is Pro, Asp, Gly, Ala, Arg, Leu, or Gln; 103 Xaa at position 32 is Leu, Val, Arg, Gln, Asn, Gly, Ala, or 104 Glu; 105 Xaa at position 33 is Pro, Leu, Gln, Ala, Thr, or Glu; 106 Xaa at position 34 is Leu, Val, Gly, Ser, Lys, Glu, Gln, Thr, 107 Arg, Ala, Phe, Ile or Met; 108 Xaa at position 35 is Leu, Ala, Gly, Asn, Pro, Gln, or Val; 109 Xaa at position 36 is Asp, Leu, or Val; 110 Xaa at position 37 is Phe, Ser, Pro, Trp, or Ile; 111 Xaa at position 38 is Asn, or Ala; 112 Xaa at position 40 is Leu, Trp, or Arg; 113 Xaa at position 41 is Asn, Cys, Arg, Leu, His, Met, or Pro; 114 Xaa at position 42 is Gly, Asp, Ser, Cys, Asn, Lys, Thr, Leu, 115 Val, Glu, Phe, Tyr, Ile, Met or Ala; 116 Xaa at position 43 is Glu, Asn, Tyr, Leu, Phe, Asp, Ala, Cys, 117 Gln, Arg, Thr, Gly or Ser; 118 Xaa at position 44 is Asp, Ser, Leu, Arg, Lys, Thr, Met, Trp,

Xaa at position 45 is Gln, Pro, Phe, Val, Met, Leu, Thr, Lys,

Glu, Asn, Gln, Ala or Pro;

155

His;

121 Trp, Asp, Asn, Arg, Ser, Ala, Ile, Glu or His; 122 Xaa at position 46 is Asp, Phe, Ser, Thr, Cys, Glu, Asn, Gln, 123 Lys, His, Ala, Tyr, Ile, Val or Gly; 124 Xaa at position 47 is Ile, Gly, Val, Ser, Arg, Pro, or His; 125 Xaa at position 48 is Leu, Ser, Cys, Arg, Ile, His, Phe, Glu, 126 Lys, Thr, Ala, Met, Val or Asn; 127 Xaa at position 49 is Met, Arg, Ala, Gly, Pro, Asn, His, or 128 Asp; Xaa at position 50 is Glu, Leu, Thr, Asp, Tyr, Lys, Asn, Ser, 129 130 Ala, Ile, Val, His, Phe, Met or Gln; 131 Xaa at position 51 is Asn, Arg, Met, Pro, Ser, Thr, or His; Xaa at position 52 is Asn, His, Arg, Leu, Gly, Ser, or Thr; 132 133 Xaa at position 53 is Leu, Thr, Ala, Gly, Glu, Pro, Lys, Ser, 134 or Met; 135 Xaa at position 54 is Arg, Asp, Ile, Ser, Val, Thr, Gln, Asn, 136 Lys, His, Ala or Leu; 137 Xaa at position 55 is Arg, Thr, Val, Ser, Leu, or Gly; 138 Xaa at position 56 is Pro, Gly, Cys, Ser, Gln, Glu, Arg, His, 139 Thr, Ala, Tyr, Phe, Leu, Val or Lys; 140 Xaa at position 57 is Asn or Gly; 141 Xaa at position 58 is Leu, Ser, Asp, Arg, Gln, Val, or Cys; 142 Xaa at position 59 is Glu Tyr, His, Leu, Pro, or Arg; 143 Xaa at position 60 is Ala, Ser, Pro, Tyr, Asn, or Thr; 144 Xaa at position 61 is Phe, Asn, Glu, Pro, Lys, Arg, or Ser; 145 Xaa at position 62 is Asn, His, Val, Arg, Pro, Thr, Asp, or 146 147 Xaa at position 63 is Arg, Tyr, Trp, Lys, Ser, His, Pro, or 148 Val; 149 Xaa at position 64 is Ala, Asn, Pro, Ser, or Lys; 150 Xaa at position 65 is Val, Thr, Pro, His, Leu, Phe, or Ser; 151 Xaa at position 66 is Lys, Ile, Arg, Val, Asn, Glu, or Ser; 152 Xaa at position 67 is Ser, Ala, Phe, Val, Gly, Asn, Ile, Pro, 153 or His;

Xaa at position 68 is Leu, Val, Trp, Ser, Ile, Phe, Thr, or

- 156 Xaa at position 69 is Gln, Ala, Pro, Thr, Glu, Arg, Trp, Gly,
- 157 or Leu;
- 158 Xaa at position 70 is Asn, Leu, Val, Trp, Pro, or Ala;
- 159 Xaa at position 71 is Ala, Met, Leu, Pro, Arg, Glu, Thr, Gln,
- 160 Trp, or Asn;
- 161 Xaa at position 72 is Ser, Glu, Met, Ala, His, Asn, Arg, or
- 162 Asp;
- 163 Xaa at position 73 is Ala, Glu, Asp, Leu, Ser, Gly, Thr, or
- 164 Arg;
- 165 Xaa at position 74 is Ile, Met, Thr, Pro, Arg, Gly, Ala;
- 166 Xaa at position 75 is Glu, Lys, Gly, Asp, Pro, Trp, Arg, Ser,
- 167 Gln, or Leu;
- 168 Xaa at position 76 is Ser, Val, Ala, Asn, Trp, Glu, Pro, Gly,
- 169 or Asp;
- 170 Xaa at position 77 is Ile, Ser, Arg, Thr, or Leu;
- 171 Xaa at position 78 is Leu, Ala, Ser, Glu, Phe, Gly, or Arg;
- 172 Xaa at position 79 is Lys, Thr, Asn, Met, Arg, Ile, Gly, or
- 173 Asp;
- 174 Xaa at position 80 is Asn, Trp, Val, Gly, Thr, Leu, Glu, or
- 175 Arg;
- 176 Xaa at position 81 is Leu, Gln, Gly, Ala, Trp, Arg, Val, or
- 177 Lys;
- 178 Xaa at position 82 is Leu, Gln, Lys, Trp, Arg, Asp, Glu, Asn,
- His, Thr, Ser, Ala, Tyr, Phe, Ile, Met or Val;
- 180 Xaa at position 83 is Pro, Ala, Thr, Trp, Arg, or Met;
- 181 Xaa at position 84 is Cys, Glu, Gly, Arg, Met, or Val;
- 182 Xaa at position 85 is Leu, Asn, Val, or Gln;
- 183 Xaa at position 86 is Pro, Cys, Arg, Ala, or Lys;
- 184 Xaa at position 87 is Leu, Ser, Trp, or Gly;
- 185 Xaa at position 88 is Ala, Lys, Arg, Val, or Trp;
- 186 Xaa at position 89 is Thr, Asp, Cys, Leu, Val, Glu, His, Asn,
- 187 or Ser;
- 188 Xaa at position 90 is Ala, Pro, Ser, Thr, Gly, Asp, Ile, or
- 189 Met;
- 190 Xaa at position 91 is Ala, Pro, Ser, Thr, Phe, Leu, Asp, or
- 191 His;

- 192 Xaa at position 92 is Pro, Phe, Arg, Ser, Lys, His, Ala, Gly,
- 193 Ile or Leu;
- 194 Xaa at position 93 is Thr, Asp, Ser, Asn, Pro, Ala, Leu, or
- 195 Arg;
- 196 Xaa at position 94 is Arg, Ile, Ser, Glu, Leu, Val, Gln, Lys,
- 197 His, Ala, or Pro;
- 198 Xaa at position 95 is His, Gln, Pro, Arg, Val, Leu, Gly, Thr,
- 199 Asn, Lys, Ser, Ala, Trp, Phe, Ile, or Tyr;
- 200 Xaa at position 96 is Pro, Lys, Tyr, Gly, Ile, or Thr;
- 201 Xaa at position 97 is Ile, Val, Lys, Ala, or Asn;
- 202 Xaa at position 98 is His, Ile, Asn, Leu, Asp, Ala, Thr,
- Glu, Gln, Ser, Phe, Met, Val, Lys, Arg, Tyr or Pro;
- 204 Xaa at position 99 is Ile, Leu, Arg, Asp, Val, Pro, Gln,
- 205 Gly, Ser, Phe, or His;
- 206 Xaa at position 100 is Lys, Tyr, Leu, His, Arg, Ile, Ser, Gln,
- 207 or Pro;
- 208 Xaa at position 101 is Asp, Pro, Met, Lys, His, Thr, Val,
- 209 Tyr, Glu, Asn, Ser, Ala, Gly, Ile, Leu, or Gln;
- 210 Xaa at position 102 is Gly, Leu, Glu, Lys, Ser, Tyr, or Pro;
- 211 Xaa at position 103 is Asp, or Ser;
- 212 Xaa at position 104 is Trp, Val, Cys, Tyr, Thr, Met, Pro, Leu,
- 213 Gln, Lys, Ala, Phe, or Gly;
- 214 Xaa at position 105 is Asn, Pro, Ala, Phe, Ser, Trp, Gln, Tyr,
- 215 Leu, Lys, Ile, Asp, or His;
- 216 Xaa at position 106 is Glu, Ser, Ala, Lys, Thr, Ile, Gly, or
- 217 Pro;
- 218 Xaa at position 108 is Arg, Lys, Asp, Leu, Thr, Ile, Gln, His,
- 219 Ser, Ala or Pro;
- 220 Xaa at position 109 is Arg, Thr, Pro, Glu, Tyr, Leu, Ser, or
- 221 Gly;
- 222 Xaa at position 110 is Lys, Ala, Asn, Thr, Leu, Arg, Gln, His,
- 223 Glu, Ser, or Trp;
- 224 Xaa at position 111 is Leu, Ile, Arg, Asp, or Met;
- 225 Xaa at position 112 is Thr, Val, Gln, Tyr, Glu, His, Ser, or
- 226 Phe;
- 227 Xaa at position 113 is Phe, Ser, Cys, His, Gly, Trp, Tyr, Asp,

- 228 Lys, Leu, Ile, Val or Asn; 229 Xaa at position 114 is Tyr, Cys, His, Ser, Trp, Arg, or Leu; 230 Xaa at position 115 is Leu, Asn, Val, Pro, Arg, Ala, His, Thr, 231 Trp, or Met; Xaa at position 116 is Lys, Leu, Pro, Thr, Met, Asp, Val, Glu, 232 233 Arg, Trp, Ser, Asn, His, Ala, Tyr, Phe, Gln, or Ile; 234 Xaa at position 117 is Thr, Ser, Asn, Ile, Trp, Lys, or Pro; 235 Xaa at position 118 is Leu, Ser, Pro, Ala, Glu, Cys, Asp, or 236 Tyr; 237 Xaa at position 119 is Glu, Ser, Lys, Pro, Leu, Thr, Tyr, or 238 239 Xaa at position 120 is Asn, Ala, Pro, Leu, His, Val, or Gln; 240 Xaa at position 121 is Ala, Ser, Ile, Asn, Pro, Lys, Asp, or 241 Gly; 242 Xaa at position 122 is Gln, Ser, Met, Trp, Arg, Phe, Pro, His, 243 Ile, Tyr, or Cys; 244 Xaa at position 123 is Ala, Met, Glu, His, Ser, Pro, Tyr, or 245 Leu, 246 247 wherein from 1 to 14 amino acids can optionally be deleted 248 from the N-terminus and/or from 1 to 15 amino acids can 249 optionally be deleted from the C-terminus of said modified 250 human interleukin-3 amino acid sequence; and wherein from 1 to 251 44 of the amino acids designated by Xaa are different from the 252 corresponding amino acids of native (1-133) human interleukin-253 3; 254 255 wherein L1 is a linker capable of linking R1 to R2; and 256 257 said hematopoietic protein can optionally be immediately preceded by  $(methionine^{-1})$ ,  $(alanine^{-1})$  or  $(methionine^{-2})$ , 258 alanine $^{-1}$ ). 259
  - 1 11. The hematopoeitic protein of claim 8 or 10 wherein  $R_2$  is 2 selected from the group consisting of:

Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Ala Glu Asp Val Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe Val Arq Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln (SEQ ID NO:225); Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Asn Pro Leu Leu Asp Pro Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Thr Pro Asn Leu Leu Ala Phe Val Arg Ala Val Lys His Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arq Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gln (SEQ ID NO:226); Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Val Pro Pro Ala Pro Leu Leu Asp Ser Asn Asn Leu Asn Ser Glu Asp Met Asp Ile Leu Met Glu Arg Asn Leu Arg Leu Pro Asn Leu Leu Ala Phe Val Arq Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Lys Ala Gly Asp

Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu

```
51
52
    Glu Gln Ala Gln Glu Gln (SEQ ID NO:227); and
53
54
    Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg
55
    Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp
56
    Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu
57
    Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile
58
    Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr
59
    Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp
60
    Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu
61
    Gln Ala Gln Glu Gln Gln (SEQ ID NO:228).
 1
         12.
              A hematopoietic protein comprising; an amino acid sequence
2
    of the formula:
 3
 4
              R_1-L_1-R_2, R_2-L_1-R_1, R_1-R_2, or R_2-R_1
 5
 6
         wherein R1 is a polypeptide comprising; a modified human
 7
    c-mpl ligand amino acid sequence of the formula:
 8
9
    SerProAlaProProAlaCysAspLeuArgValLeuSerLysLeuLeuArgAspSer
10
                                10
11
12
    HisValLeuHisSerArgLeuSerGlnCysProGluValHisProLeuProThrPro
13
                    25
                                    30
14
15
    ValLeuLeuProAlaValAspPheSerLeuGlyGluTrpLysThrGlnMetGluGlu
16
       40
                       45
                                       50
                                                       55
17
18
    ThrLysAlaGlnAspIleLeuGlyAlaValThrLeuLeuLeuGluGlyValMetAla
19
          60
                          65
                                                          75
20
21
    AlaArgGlyGlnLeuGlyProThrCysLeuSerSerLeuLeuGlyGlnLeuSerGly
22
             80
                             85
                                             90
                                                             95
23
24
    GlnValArgLeuLeuGlyAlaLeuGlnSerLeuLeuGlyThrGlnXaaXaaXaa
25
                                105
                                                110
26
27
    XaaGlyArgThrThrAlaHisLysAspProAsnAlaIlePheLeuSerPheGlnHis
28
                    120
                                   125
29
30
    LeuLeuArgGlyLysValArgPheLeuMetLeuValGlyGlySerThrLeuCysVal
```

Arg (SEQ ID NO:256) wherein Xaa at position 112 is deleted or Leu, Ala, Val, Ile, Pro, Phe, Trp, or Met; Xaa at position 113 is deleted or Pro, Phe, Ala, Val, Leu, Ile, Trp, or Met; Xaa at position 114 is deleted or Pro, Phe, Ala, Val, Ile, Trp, or Met; Xaa at position 115 is deleted or Gln, Gly, Ser, Thr, Asn; and wherein the N-terminus is joined to the C-terminus directly or

through a linker (L2) capable of joining the N-terminus to the

C-terminus and having new C- and N-termini at amino acids:

26-27	51-52	108-109
27-28	52-53	109-110
28-29	53-54	110-111
29-30	54-55	111-112
30-31	55-56	112-113
32-33	56-57	113-114
33-34	57-58	114-115
34-35	58-59	115-116
36-37	59-60	116-117
37-38	78-79	117-118
38-39	79-80	118-119
40-41	80-81	119-120
41-42	81-82	120-121
42-43	82-83	121-122
43-44	83-84	122-123
44-45	84-85	123-124
46-47	85-86	124-125
47-48	86-87	125-126
48-49	87-88	126-127

```
50-51
                                             or 127-128
                        88-89
                                             respectively;
51
         wherein R_2 is G-CSF or G-CSF Ser^{17}
52
53
54
         wherein L<sub>1</sub> is a linker capable of linking R<sub>1</sub> to R<sub>2</sub>; and
55
56
         said hematopoietic protein can optionally be immediately
57
    preceded by (methionine^{-1}), (alanine^{-1}) or (methionine^{-2}),
58
    alanine^{-1}).
1
              The hematopoietic protein as recited in claim 1, 2,
         13.
2
    3, 4, 5, 6, 7, 8, 9, 10 or 12 wherein said linker (L2) is
3
    selected from the group consisting of;
4
         GlyGlyGlySer (SEQ ID NO:12);
5
         GlyGlyGlySerGlyGlySer (SEQ ID NO:242);
6
         GlyGlyGlySerGlyGlySerGlyGlySer
7
         (SEQ ID NO:243);
8
         SerGlyGlySerGlyGlySer (SEQ ID NO:244);
9
         GluPheGlyAsnMetAla (SEQ ID NO:245);
10
         GluPheGlyGlyAsnMetAla (SEQ ID NO:246);
11
         GluPheGlyGlyAsnGlyGlyAsnMetAla (SEQ ID NO:247); and
12
         GlyGlySerAspMetAlaGly (SEQ ID NO:248).
1
              The hematopoietic protein as recited in claim 11
    wherein said linker (L2) is selected from the group consisting
2
3
    of:
4
         GlyGlyGlySer (SEQ ID NO:12);
5
         GlyGlyGlySerGlyGlySer (SEQ ID NO:242);
6
         GlyGlyGlySerGlyGlySerGlyGlySer
7
         (SEQ ID NO:243);
8
         SerGlyGlySerGlyGlySer (SEQ ID NO:244);
9
         GluPheGlyAsnMetAla (SEQ ID NO:245);
10
         GluPheGlyGlyAsnMetAla (SEQ ID NO:246);
11
         GluPheGlyGlyAsnGlyGlyAsnMetAla (SEQ ID NO:247); and
12
         GlyGlySerAspMetAlaGly (SEQ ID NO:248).
```

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44

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1 The hematopoietic protein as recited in claim 1 15. 2 wherein said protein is selected from the group consisting of: 3 4 5 Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp 6 7 Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu 8 Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile 9 Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr 10 Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu 11 12 Gln Ala Gln Glu Gln Gln Tyr Val Glu Gly Gly Gly Ser Pro 13 Gly Gly Gly Ser Gly Gly Ser Asn Met Ala Tyr Lys Leu Cys 14 His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro 15 Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala 16 Gly Cys Leu Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly 17 Leu Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr 18 Leu Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile 19 Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro 20 Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu 21 22 Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro Ser Gly Gly 23 Ser Gly Gly Ser Gln Ser Phe Leu Leu Lys Ser Leu Glu Gln Val 24 Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys 25 Ala Thr (SEQ ID NO:166); 26 27 28 Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg 29 Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp 30 Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile 31 32 Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr 33 Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp 34 Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu 35 Gln Ala Gln Glu Gln Tyr Val Glu Gly Gly Gly Ser Pro 36 Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro 37 Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Tyr Lys Leu Cys 38 His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro 39 Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala 40 Gly Cys Leu Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly

Leu Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr

Leu Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile

Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro

Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg

Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu

Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro Ser Gly Gly

Ser Gly Gly Ser Gln Ser Phe Leu Leu Lys Ser Leu Glu Gln Val

48 Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys 49 Ala Thr (SEQ ID NO:167); 50

51 52

53

54

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56

57

58

59

60

61

62

63 64

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66 67

68

69

70

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72

Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Tyr Val Glu Gly Gly Gly Ser Pro Gly Gly Gly Ser Gly Gly Ser Asn Met Ala Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro Ser Gly Gly Ser Gly Gly Ser Gln Ser Phe Leu Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser (SEQ ID NO:168);

73 74

75 Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arq 76 Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp 77 Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu 78 Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile 79 Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr 80 Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu 81 82 Gln Ala Gln Gln Gln Tyr Val Glu Gly Gly Gly Ser Pro 83 Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro 84 Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Pro Glu Leu Gly 85 Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr 86 Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu 87 Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln 88 Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe 89 Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro Ser Gly Gly Ser Gly Ser Gln Ser Phe Leu Leu Lys Ser Leu Glu 90 91 Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys 92 Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu 93 Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys 94 Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His 95 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly 96 Ile Ser (SEQ ID NO:169);
97

98

99 Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg 100 Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp 101 Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu 102 Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile 103 Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr 104 Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp 105 Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu 106 Gln Ala Gln Glu Gln Gln Tyr Val Glu Gly Gly Gly Ser Pro 107 Gly Gly Gly Ser Gly Gly Ser Asn Met Ala Met Ala Pro Ala 108 Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe 109 Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro 110 111 Ser Gly Gly Ser Gly Ser Gln Ser Phe Leu Leu Lys Ser Leu 112 Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu 113 Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val 114 Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser 115 Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu 116 His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu 117 Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu 118 Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu 119 Leu Gly (SEQ ID NO:170);

120 121

122 Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arq 123 Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp 124 Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile 125 126 Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr 127 Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp 128 Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu 129 Gln Ala Gln Glu Gln Tyr Val Glu Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro 130 131 Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Met Ala Pro Ala 132 Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe 133 Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser 134 Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro 135 Ser Gly Gly Ser Gly Ser Gln Ser Phe Leu Leu Lys Ser Leu 136 Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu 137 Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val 138 Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser 139 Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu 140 141 Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu

142 Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu 143 Leu Gly (SEQ ID NO:171);
144

145

146 Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg 147 Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp 148 Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu 149 Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile 150 Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr 151 Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp 152 Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu 153 Gln Ala Gln Glu Gln Gln Tyr Val Glu Gly Gly Gly Ser Pro 154 Gly Gly Gly Ser Gly Gly Ser Asn Met Ala Thr Gln Gly Ala 155 Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val 156 Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg 157 Val Leu Arg His Leu Ala Gln Pro Ser Gly Gly Ser Gly Gly Ser 158 Gln Ser Phe Leu Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln 159 Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys 160 Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly 161 Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln 162 Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly 163 164 Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr 165 Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu 166 Gln Pro (SEQ ID NO:172);

167 168

169 Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arq 170 Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu 171 172 Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile 173 Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr 174 Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp 175 Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu 176 Gln Ala Gln Glu Gln Tyr Val Glu Gly Gly Gly Ser Pro 177 Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro 178 Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Thr Gln Gly Ala 179 Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val 180 Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg 181 Val Leu Arg His Leu Ala Gln Pro Ser Gly Gly Ser Gly Gly Ser 182 Gln Ser Phe Leu Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys 183 Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly 184 185 Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln 186 Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu Phe Leu Tyr 187 Gln Gly Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly 188 Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr

189 Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu 190 Gln Pro (SEQ ID NO:173);
191

192

193 Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg 194 Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp 195 Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu 196 Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile 197 Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr 198 Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp 199 Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu 200 Gln Ala Gln Glu Gln Gln Tyr Val Glu Gly Gly Gly Ser Pro 201 Gly Gly Gly Ser Gly Gly Ser Asn Met Ala Ser Ala Phe Gln 202 Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe 203 Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro Ser 204 Gly Gly Ser Gly Gly Ser Gln Ser Phe Leu Leu Lys Ser Leu Glu 205 Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys 206 Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu 207 Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys 208 Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His 209 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly 210 Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp 211 Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu 212 Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala 213 Phe Ala (SEQ ID NO:177);

214215

216 Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arq 217 Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp 218 Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile 219 220 Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr 221 Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp 222 Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu 223 Gln Ala Gln Glu Gln Tyr Val Glu Gly Gly Gly Ser Pro 224 Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro 225 Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Ser Ala Phe Gln 226 Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe 227 Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro Ser 228 Gly Gly Ser Gly Ser Gln Ser Phe Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys 229 230 Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu 231 Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His 232 233 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly 234 Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp 235 Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu 236 Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala 237 Phe Ala (SEQ ID NO:175); 238

239

240 Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg 241 Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu 242 243 Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile 244 Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr 245 Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp 246 Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu 247 Gln Ala Gln Glu Gln Tyr Val Glu Gly Gly Gly Ser Pro 248 Gly Gly Gly Ser Gly Gly Ser Asn Met Ala Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro 249 250 Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala 251 Gly Cys Leu Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly 252 Leu Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr 253 Leu Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile 254 Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro 255 Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg 256 Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu 257 Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro Thr Pro Leu 258 Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Ser Leu 259 Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu 260 Lys Leu Cys Ala Thr (SEQ ID NO:176);

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263 Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg 264 Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp 265 Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile 266 267 Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr 268 Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp 269 Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu 270 Gln Ala Gln Glu Gln Gln Tyr Val Glu Gly Gly Gly Ser Pro 271 Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro 272 Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Tyr Lys Leu Cys 273 His Pro Glu Glu Leu Val Leu Gly His Ser Leu Gly Ile Pro 274 Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala 275 Gly Cys Leu Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly 276 Leu Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr 277 Leu Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro 278 279 Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg 280 Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu 281 Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro Thr Pro Leu 282 Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Ser Leu 283 Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu 284 Lys Leu Cys Ala Thr (SEQ ID NO:177); 285

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287 Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg 288 Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu 289 290 Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile 291 Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr 292 Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp 293 Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu 294 Gln Ala Gln Glu Gln Gln Tyr Val Glu Gly Gly Gly Ser Pro 295 Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro 296 Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Pro Glu Leu Gly 297 Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr 298 Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu 299 Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln 300 Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe 301 Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro Thr 302 Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu 303 304 Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu 305 Leu Val Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser 306 307 Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala 308 Leu Glu Gly Ile Ser (SEQ ID NO:179);

309 310

311 Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg 312 Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp 313 Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu 314 Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile 315 Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr 316 Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp 317 Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Tyr Val Glu Gly Gly Gly Ser Pro 318 319 Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro 320 Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Met Ala Pro Ala 321 Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe 322 Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser 323 Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro 324 Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu 325 Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala 326 Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu 327 Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro 328 Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu 329 Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln

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330 Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr 331 Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly (SEQ ID NO:181); 332 333 334 335 Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg 336 Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp 337 Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu 338 Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile 339 Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr 340 Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp 341 Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu 342 Gln Ala Gln Glu Gln Gln Tyr Val Glu Gly Gly Gly Ser Pro Gly Gly Gly Ser Gly Gly Ser Asn Met Ala Thr Gln Gly Ala 343 344 Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg 345 346 Val Leu Arg His Leu Ala Gln Pro Thr Pro Leu Gly Pro Ala Ser 347 Ser Leu Pro Gln Ser Phe Leu Leu Lys Ser Leu Glu Gln Val Arg 348 Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala 349 Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His 350 Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln 351 Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu 352 Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser Pro 353 Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp 354 Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala 355 Pro Ala Leu Gln Pro (SEQ ID NO:182); 356 357 358 Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg 359 Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu 360 361 Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile 362 Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr 363 Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp 364 Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Tyr Val Glu Gly Gly Gly Ser Pro 365 366 Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Thr Gln Gly Ala 367 Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val 368 369 Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg 370 Val Leu Arg His Leu Ala Gln Pro Thr Pro Leu Gly Pro Ala Ser 371 Ser Leu Pro Gln Ser Phe Leu Leu Lys Ser Leu Glu Gln Val Arq 372 Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala 373 Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His

Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln

Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu

Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser Pro

377 Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp 378 Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala 379 Pro Ala Leu Gln Pro (SEQ ID NO:183);

380 381

382 Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg 383 Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp 384 Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu 385 Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile 386 Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr 387 Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu 388 Gln Ala Gln Glu Gln Tyr Val Glu Gly Gly Gly Ser Pro 389 390 Gly Gly Gly Ser Gly Gly Ser Asn Met Ala Ser Ala Phe Gln 391 Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro Thr 392 393 Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys 394 Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu 395 Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu 396 Leu Val Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser 397 398 Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala 399 Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met 400 401 Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala 402 Met Pro Ala Phe Ala (SEQ ID NO:184);

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MetAlaAsnCysSerIleMetIleAspGluIleIleHisHisLeuLysArgProProAla  ${\tt ProLeuLeuAspProAsnAsnLeuAsnAspGluAspValSerIleLeuMetAspArgAsn}$ LeuArgLeuProAsnLeuGluSerPheValArgAlaValLysAsnLeuGluAsnAlaSer GlyIleGluAlaIleLeuArgAsnLeuGlnProCysLeuProSerAlaThrAlaAlaPro SerArgHisProIleIleIleLysAlaGlyAspTrpGlnGluPheArgGluLysLeuThr PheTyrLeuValThrLeuGluGlnAlaGlnGluGlnGlnTyrValGluGlyGlyGlyGly SerProGlyGluProSerGlyProIleSerThrIleAsnProSerProProSerLysGlu SerHisLysSerProAsnMetAlaTyrLysLeuCysHisProGluGluLeuValLeuLeu GlyHisSerLeuGlyIleProTrpAlaProLeuSerSerCysProSerGlnAlaLeuGln LeuAlaGlyCysLeuSerGlnLeuHisSerGlyLeuPheLeuTyrGlnGlyLeuLeuGln AlaLeuGluGlyIleSerProGluLeuGlyProThrLeuAspThrLeuGlnLeuAspVal AlaAspPheAlaThrThrIleTrpGlnGlnMetGluGluLeuGlyMetAlaProAlaLeu GlnProThrGlnGlyAlaMetProAlaPheAlaSerAlaPheGlnArqArqAlaGlyGly ValLeuValAlaSerHisLeuGlnSerPheLeuGluValSerTyrArqValLeuArqHis LeuAlaGlnProGlyGlyGlySerAspMetAlaThrProLeuGlyProAlaSerSerLeu ProGlnSerPheLeuLeuLysSerLeuGluGlnValArqLysIleGlnGlyAspGlyAla AlaLeuGlnGluLysLeuCysAlaThr (SEQ ID NO:194);

424 MetAlaAsnCysSerIleMetIleAspGluIleIleHisHisLeuLysArgProProAla 425 ProLeuLeuAspProAsnAsnLeuAsnAspGluAspValSerIleLeuMetAspArgAsn 426 LeuArgLeuProAsnLeuGluSerPheValArgAlaValLysAsnLeuGluAsnAlaSer 427 GlyIleGluAlaIleLeuArqAsnLeuGlnProCysLeuProSerAlaThrAlaAlaPro 428 SerArgHisProIleIleIleLysAlaGlyAspTrpGlnGluPheArgGluLysLeuThr 429 PheTyrLeuValThrLeuGluGlnAlaGlnGluGlnGlnTyrValGluGlyGlyGlyGly 430 SerProGlyGluProSerGlyProIleSerThrIleAsnProSerProProSerLysGlu SerHisLysSerProAsnMetAlaProGluLeuGlyProThrLeuAspThrLeuGlnLeu 431 432 AspValAlaAspPheAlaThrThrIleTrpGlnGlnMetGluGluLeuGlvMetAlaPro 433 AlaLeuGlnProThrGlnGlyAlaMetProAlaPheAlaSerAlaPheGlnArgArgAla 434 GlyGlyValLeuValAlaSerHisLeuGlnSerPheLeuGluValSerTyrArqValLeu 435 ArgHisLeuAlaGlnProGlyGlyGlySerAspMetAlaThrProLeuGlyProAlaSer 436 SerLeuProGlnSerPheLeuLeuLysSerLeuGluGlnValArqLysIleGlnGlyAsp GlyAlaAlaLeuGlnGluLysLeuCysAlaThrTyrLysLeuCysHisProGluGluLeu 437 438 ValLeuLeuGlyHisSerLeuGlyIleProTrpAlaProLeuSerSerCysProSerGln 439 AlaLeuGlnLeuAlaGlyCysLeuSerGlnLeuHisSerGlyLeuPheLeuTyrGlnGly 440 LeuLeuGlnAlaLeuGluGlyIleSer (SEQ ID NO:195);

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MetAlaAsnCysSerIleMetIleAspGluIleIleHisHisLeuLysArgProProAla ProLeuLeuAspProAsnAsnLeuAsnAspGluAspValSerIleLeuMetAspArgAsn LeuArqLeuProAsnLeuGluSerPheValArqAlaValLysAsnLeuGluAsnAlaSer GlyIleGluAlaIleLeuArgAsnLeuGlnProCysLeuProSerAlaThrAlaAlaPro SerArgHisProIleIleIleLysAlaGlyAspTrpGlnGluPheArgGluLysLeuThr PheTyrLeuValThrLeuGluGlnAlaGlnGluGlnGlnTyrValGluGlyGlyGlyGly SerProGlyGluProSerGlyProIleSerThrIleAsnProSerProProSerLysGlu SerHisLysSerProAsnMetAlaSerAlaPheGlnArgArgAlaGlyGlyValLeuVal AlaSerHisLeuGlnSerPheLeuGluValSerTyrArqValLeuArqHisLeuAlaGln ProGlyGlyGlySerAspMetAlaThrProLeuGlyProAlaSerSerLeuProGlnSer PheLeuLeuLysSerLeuGluGlnValArqLysIleGlnGlyAspGlyAlaAlaLeuGln GluLysLeuCysAlaThrTyrLysLeuCysHisProGluGluLeuValLeuLeuGlyHis SerLeuGlyIleProTrpAlaProLeuSerSerCysProSerGlnAlaLeuGlnLeuAla GlyCysLeuSerGlnLeuHisSerGlyLeuPheLeuTyrGlnGlyLeuLeuGlnAlaLeu GluGlyIleSerProGluLeuGlyProThrLeuAspThrLeuGlnLeuAspValAlaAsp  $\label{lem:pheAlaThrThrIleTrpGlnGlnMetGluGluLeuGlyMetAlaProAlaLeuGlnProPheAlaThrThrIleTrpGlnGlnMetGluGluLeuGlyMetAlaProAlaLeuGlnProPheAlaThrThrIleTrpGlnGlnMetGluGluLeuGlyMetAlaProAlaLeuGlnProPheAlaThrThrIleTrpGlnGlnMetGluGluLeuGlyMetAlaProAlaLeuGlnProPheAlaThrThrIleTrpGlnGlnMetGluGluLeuGlyMetAlaProAlaLeuGlnProPheAlaThrThrIleTrpGlnGlnMetGluGluLeuGlyMetAlaProAlaLeuGlnProPheAlaThrThrIleTrpGlnGlnMetGluGluLeuGlyMetAlaProAlaLeuGlnProPheAlaThrThrIleTrpGlnGlnMetGluGluLeuGlyMetAlaProAlaLeuGlnProPheAlaThrThrIleTrpGlnGlnMetGluGluLeuGlyMetAlaProAlaLeuGlnProPheAlaThrThrIleTrpGlnGlnMetGluGluLeuGlyMetAlaProAlaLeuGlnProPheAlaThrThrIleTrpGlnGlnMetGluGluLeuGlyMetAlaProAlaLeuGlnProPheAlaThrThrIleTrpGlnGlnMetGluGluLeuGlyMetAlaProAlaLeuGlnProPheAlaThrThrIleTrpGlnGlnMetGluGluCeuGlyMetAlaProAlaThrThrIleTrpGlnGlnMetGluGluCeuGlyMetAlaProAlaChuGlyMetAlaProAlaChuGlyMetAlaProAlaChuGlyMetAlaProAlaChuGlyMetAlaProAlaChuGlyMetAlaProAlaChuGlyMetAlaProAlaChuGlyMetAlaProAlaChuGlyMetAlaProAlaChuGlyMetAlaChuGl$ ThrGlnGlyAlaMetProAlaPheAla (SEQ ID NO:196);

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MetAlaAsnCysSerIleMetIleAspGluIleIleHisHisLeuLysArgProProAla ProLeuLeuAspProAsnAsnLeuAsnAspGluAspValSerIleLeuMetAspArgAsn LeuArgLeuProAsnLeuGluSerPheValArgAlaValLysAsnLeuGluAsnAlaSer GlyIleGluAlaIleLeuArgAsnLeuGlnProCysLeuProSerAlaThrAlaAlaPro SerArgHisProIleIleIleLysAlaGlyAspTrpGlnGluPheArgGluLysLeuThr PheTyrLeuValThrLeuGluGlnAlaGlnGluGlnGlnTyrValGluGlyGlyGlyGly SerProGlyGluProSerGlyProIleSerThrIleAsnProSerProProSerLysGlu SerHisLysSerProAsnMetAlaMetAlaProAlaLeuGlnProThrGlnGlyAlaMet ProAlaPheAlaSerAlaPheGlnArgArgAlaGlyGlyValLeuValAlaSerHisLeu

471 GlnSerPheLeuGluValSerTyrArgValLeuArgHisLeuAlaGlnProGlyGlyGly 472 SerAspMetAlaThrProLeuGlyProAlaSerSerLeuProGlnSerPheLeuLeuLys 473 SerLeuGluGlnValArgLysIleGlnGlyAspGlyAlaAlaLeuGlnGluLysLeuCys 474 AlaThrTyrLysLeuCysHisProGluGluLeuValLeuGlyHisSerLeuGlyIle 475 ProTrpAlaProLeuSerSerCysProSerGlnAlaLeuGlnLeuAlaGlyCysLeuSer 476 GlnLeuHisSerGlyLeuPheLeuTyrGlnGlyLeuLeuGlnAlaLeuGluGlyIleSer 477 ProGluLeuGlyProThrLeuAspThrLeuGlnLeuAspValAlaAspPheAlaThrThr 478 IleTrpGlnGlnMetGluGluLeuGly (SEQ ID NO:197);

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MetAlaAsnCysSerIleMetIleAspGluIleIleHisHisLeuLysArgProProAla ProLeuLeuAspProAsnAsnLeuAsnAspGluAspValSerIleLeuMetAspArgAsn LeuArgLeuProAsnLeuGluSerPheValArgAlaValLysAsnLeuGluAsnAlaSer GlyIleGluAlaIleLeuArgAsnLeuGlnProCysLeuProSerAlaThrAlaAlaPro SerArgHisProIleIleIleLysAlaGlyAspTrpGlnGluPheArgGluLysLeuThr PheTyrLeuValThrLeuGluGlnAlaGlnGluGlnGlnTyrValGluGlyGlyGlyGly SerProGlyGluProSerGlyProIleSerThrIleAsnProSerProProSerLysGlu SerHisLysSerProAsnMetAlaThrGlnGlyAlaMetProAlaPheAlaSerAlaPhe GlnArqArqAlaGlyGlyValLeuValAlaSerHisLeuGlnSerPheLeuGluValSer TyrArgValLeuArgHisLeuAlaGlnProGlyGlyGlySerAspMetAlaThrProLeu GlyProAlaSerSerLeuProGlnSerPheLeuLeuLysSerLeuGluGlnValArgLys IleGlnGlyAspGlyAlaAlaLeuGlnGluLysLeuCysAlaThrTyrLysLeuCysHis ProGluGluLeuValLeuGlyHisSerLeuGlyIleProTrpAlaProLeuSerSer CysProSerGlnAlaLeuGlnLeuAlaGlyCysLeuSerGlnLeuHisSerGlyLeuPhe LeuTyrGlnGlyLeuLeuGlnAlaLeuGluGlyIleSerProGluLeuGlyProThrLeu AspThrLeuGlnLeuAspValAlaAspPheAlaThrThrIleTrpGlnGlnMetGluGlu LeuGlyMetAlaProAlaLeuGlnPro (SEQ ID NO:198);

498 499

500 Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys 501 Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu 502 Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu 503 Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly 504 Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala 505 Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp 506 Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu 507 Glu Gln Ala Gln Glu Gln Tyr Val Glu Gly Gly Ser Pro 508 Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro 509 Ser Lys Glu Ser His Lys Ser Pro Asn Met Gly Pro Thr Cys Leu 510 Ser Ser Leu Leu Gly Gln Leu Ser Gly Gln Val Arg Leu Leu 511 Gly Ala Leu Gln Ser Leu Leu Gly Thr Gln Leu Pro Pro Gln Gly 512 Arg Thr Thr Ala His Lys Asp Pro Asn Ala Ile Phe Leu Ser Phe 513 Gln His Leu Leu Arg Gly Lys Val Arg Phe Leu Met Leu Val Gly 514 Gly Ser Thr Leu Cys Val Arg Glu Phe Gly Gly Asn Met Ala Ser 515 Pro Ala Pro Pro Ala Cys Asp Leu Arg Val Leu Ser Lys Leu Leu 516 Arg Asp Ser His Val Leu His Ser Arg Leu Ser Gln Cys Pro Glu 517 Val His Pro Leu Pro Thr Pro Val Leu Leu Pro Ala Val Asp Phe 518 Ser Leu Gly Glu Trp Lys Thr Gln Met Glu Glu Thr Lys Ala Gln 519 Asp Ile Leu Gly Ala Val Thr Leu Leu Leu Glu Gly Val Met Ala 520 Ala Arg Gly Gln Leu (SEQ ID NO:209); 521 522 523 Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys 524

Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu 530 Glu Gln Ala Gln Gln Gln Tyr Val Glu Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Gly Thr Gln Leu Pro Pro Gln Gly Arg Thr Thr Ala His Lys Asp Pro Asn Ala Ile Phe Leu Ser Phe Gln His Leu Leu Arg Gly Lys Val Arg Phe Leu Met Leu Val Gly Gly Ser Thr Leu Cys Val Arg Glu Phe Gly Gly Asn Met Ala Ser Pro Ala Pro Pro Ala Cys Asp Leu Arg Val Leu Ser Lys Leu Leu Arg Asp Ser His Val Leu His Ser Arg Leu Ser Gln Cys Pro Glu Val His Pro Leu Pro Thr Pro Val Leu Leu Pro Ala Val Asp Phe Ser Leu Gly Glu Trp Lys Thr Gln Met Glu Glu Thr 540 Lys Ala Gln Asp Ile Leu Gly Ala Val Thr Leu Leu Glu Gly Val Met Ala Ala Arg Gly Gln Leu Gly Pro Thr Cys Leu Ser Ser Leu Leu Gly Gln Leu Ser Gly Gln Val Arg Leu Leu Gly Ala Leu Gln Ser Leu Leu (SEQ ID NO:210);

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545 546 Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys 547 Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu 548 Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu 549 Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly 550 Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala 551 Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp 552 Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Tyr Val Glu Gly Gly Ser Pro 553 554 Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro 555 Ser Lys Glu Ser His Lys Ser Pro Asn Met Gly Arg Thr Thr Ala 556 His Lys Asp Pro Asn Ala Ile Phe Leu Ser Phe Gln His Leu Leu 557 Arg Gly Lys Val Arg Phe Leu Met Leu Val Gly Gly Ser Thr Leu 558 Cys Val Arg Glu Phe Gly Gly Asn Met Ala Ser Pro Ala Pro Pro 559 Ala Cys Asp Leu Arg Val Leu Ser Lys Leu Leu Arg Asp Ser His Val Leu His Ser Arg Leu Ser Gln Cys Pro Glu Val His Pro Leu 560 561 Pro Thr Pro Val Leu Leu Pro Ala Val Asp Phe Ser Leu Gly Glu 562 Trp Lys Thr Gln Met Glu Glu Thr Lys Ala Gln Asp Ile Leu Gly 563 Ala Val Thr Leu Leu Glu Gly Val Met Ala Ala Arg Gly Gln 564 Leu Gly Pro Thr Cys Leu Ser Ser Leu Leu Gly Gln Leu Ser Gly Gln Val Arg Leu Leu Gly Ala Leu Gln Ser Leu Leu Gly Thr Gln Leu Pro Pro Gln (SEQ ID NO:211);

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569 Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys 570 Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu 571 572 Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala Ser Gly 573 Ile Glu Ala Ile Leu Arq Asn Leu Gln Pro Cys Leu Pro Ser Ala 574 Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp 575 Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu 576 Glu Gln Ala Gln Glu Gln Tyr Val Glu Gly Gly Ser Pro 577 Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro 578 Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala His Lys Asp Pro 579 Asn Ala Ile Phe Leu Ser Phe Gln His Leu Leu Arg Gly Lys Val Arg Phe Leu Met Leu Val Gly Gly Ser Thr Leu Cys Val Arg Glu 580 581 Phe Gly Gly Asn Met Ala Ser Pro Ala Pro Pro Ala Cys Asp Leu 582 Arg Val Leu Ser Lys Leu Leu Arg Asp Ser His Val Leu His Ser 583 Arg Leu Ser Gln Cys Pro Glu Val His Pro Leu Pro Thr Pro Val 584 Leu Leu Pro Ala Val Asp Phe Ser Leu Gly Glu Trp Lys Thr Gln 585 Met Glu Glu Thr Lys Ala Gln Asp Ile Leu Gly Ala Val Thr Leu 586 Leu Leu Glu Gly Val Met Ala Ala Arg Gly Gln Leu Gly Pro Thr 587 Cys Leu Ser Ser Leu Leu Gly Gln Leu Ser Gly Gln Val Arg Leu 588 Leu Leu Gly Ala Leu Gln Ser Leu Leu Gly Thr Gln Leu Pro Pro 589 Gln Gly Arg Thr Thr (SEQ ID NO:212);

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592 Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp Val Ser Ile Leu Met 593 Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe Val Arg Ala 594 Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg 595 Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg 596 His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu 597 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln 598 Gln Gly Gly Ser Asn Cys Ser Ile Met Ile Asp Glu Ile Ile 599 His His Leu Lys Arg Pro Pro Ala Pro Leu Tyr Val Glu Gly Gly 600 Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn 601 Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala 602 Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg 603 Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu 604 Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro Ser Gly Gly 605 Ser Gly Gly Ser Gln Ser Phe Leu Leu Lys Ser Leu Glu Gln Val 606 Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys 607 Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly 608 His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser 609 Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly 610 Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser 611 Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met 612 613 Ala Pro Ala Leu Gln Pro (SEQ ID NO:186); 614 615 616 Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys 617 Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile 618 Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr 619 Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gly Gly Gly Ser 620 Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg 621 Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp 622 Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu 623 Ser Phe Val Arg Ala Val Lys Asn Leu Glu Tyr Val Glu Gly Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn 624 625 Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala 626 Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg 627 Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu 628 Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro Ser Gly Gly 629 Ser Gly Gly Ser Gln Ser Phe Leu Leu Lys Ser Leu Glu Gln Val 630 Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys 631 Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly 632 His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser 633 Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly 634 Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser 635 Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala 636 Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met 637 Ala Pro Ala Leu Gln Pro (SEQ ID NO:187); 638 639 640 Ala Pro Ser Arg His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln 641 Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln 642 Ala Gln Glu Gln Gly Gly Gly Ser Asn Cys Ser Ile Met Ile 643 Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Ala Pro Leu Leu 644 Asp Pro Asn Asn Leu Asn Asp Glu Asp Val Ser Ile Leu Met Asp 645 Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val 646 Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn 647 Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Tyr Val Glu Gly Gly 648 Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn 649 Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala 650 Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg 651 Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu 652 Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro Ser Gly Gly 653 Ser Gly Gly Ser Gln Ser Phe Leu Leu Lys Ser Leu Glu Gln Val 654 Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys

Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly

His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser

Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly

Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser

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Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro (SEQ ID NO:189);

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664 Leu Asp Pro Asn Asn Leu Asn Asp Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe Val Arg Ala 665 666 Val Lys Asn Leu Glu Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg 667 Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg 668 His Pro Ile Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu 669 Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln 670 Gln Gly Gly Ser Gly Gly Ser Gly Gly Ser Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro 671 672 Ala Pro Leu Tyr Val Glu Gly Gly Gly Ser Pro Gly Glu Pro 673 Ser Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu 674 Ser His Lys Ser Pro Asn Met Ala Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala 675 676 Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg 677 His Leu Ala Gln Pro Ser Gly Gly Ser Gly Gly Ser Gln Ser Phe Leu Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly 678 679 Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His 680 Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp 681 Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly 682 Cys Leu Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu 683 Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu 684 Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp 685 Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro 686 (SEQ ID NO:190);

687 688

689 Asn Ala Ser Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys 690 Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Ile 691 Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr 692 Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Gly Gly Gly Ser 693 Gly Gly Gly Ser Gly Gly Ser Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His Leu Lys Arg Pro Pro Ala Pro Leu Leu Asp 694 695 Pro Asn Asn Leu Asn Asp Glu Asp Val Ser Ile Leu Met Asp Arq 696 Asn Leu Arg Leu Pro Asn Leu Glu Ser Phe Val Arg Ala Val Lys 697 Asn Leu Glu Tyr Val Glu Gly Gly Gly Ser Pro Gly Glu Pro 698 Ser Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu 699 Ser His Lys Ser Pro Asn Met Ala Thr Gln Gly Ala Met Pro Ala 700 Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala 701 Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg 702 His Leu Ala Gln Pro Ser Gly Gly Ser Gly Gly Ser Gln Ser Phe 703 Leu Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly 704 Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His 705 Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly
Cys Leu Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu
Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu
Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp
Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro;
(SEQ ID NO:191)

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MetAlaAsnCysSerAsnMetIleAspGluIleIleThrHisLeuLysGlnProProLeu ProLeuLeuAspPheAsnAsnLeuAsnGlyGluAspGlnAspIleLeuMetAspAsnAsn LeuArgArgProAsnLeuGluAlaPheAsnArgAlaValLysSerLeuGlnAsnAlaSer AlaIleGluSerIleLeuLysAsnLeuLeuProCysLeuProLeuAlaThrAlaAlaPro ThrArgHisProIleHisIleLysAspGlyAspTrpAsnGluPheArgArgLysLeuThr PheTyrLeuLysThrLeuGluAsnAlaGlnAlaGlnGlnTyrValGluGlyGlyGlyGly SerProGlyGluProSerGlyProIleSerThrIleAsnProSerProProSerLysGlu SerHisLysSerProAsnMetAlaThrGlnGlyAlaMetProAlaPheAlaSerAlaPhe GlnArgArgAlaGlyGlyValLeuValAlaSerHisLeuGlnSerPheLeuGluValSer TyrArqValLeuArqHisLeuAlaGlnProSerGlyGlySerGlyGlySerGlnSerPhe LeuLeuLysSerLeuGluGlnValArqLysIleGlnGlyAspGlyAlaAlaLeuGlnGlu LysLeuCysAlaThrTyrLysLeuCysHisProGluGluLeuValLeuLeuGlyHisSer LeuGlyIleProTrpAlaProLeuSerSerCysProSerGlnAlaLeuGlnLeuAlaGly CysLeuSerGlnLeuHisSerGlyLeuPheLeuTyrGlnGlyLeuLeuGlnAlaLeuGlu GlyIleSerProGluLeuGlyProThrLeuAspThrLeuGlnLeuAspValAlaAspPhe AlaThrThrIleTrpGlnGlnMetGluGluLeuGlyMetAlaProAlaLeuGlnPro; (SEQ ID NO:199)

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MetAlaAsnCysSerAsnMetIleAspGluIleIleThrHisLeuLysGlnProProLeu ProLeuLeuAspPheAsnAsnLeuAsnGlyGluAspGlnAspIleLeuMetGluAsnAsn AlaIleGluSerIleLeuLysAsnLeuLeuProCysLeuProLeuAlaThrAlaAlaPro ThrArgHisProIleIleIleArgAspGlyAspTrpAsnGluPheArgArgLysLeuThr PheTyrLeuLysThrLeuGluAsnAlaGlnAlaGlnGlnTyrValGluGlyGlyGlyGly SerProGlyGluProSerGlyProIleSerThrIleAsnProSerProProSerLysGlu SerHisLysSerProAsnMetAlaThrGlnGlyAlaMetProAlaPheAlaSerAlaPhe GlnArgArgAlaGlyGlyValLeuValAlaSerHisLeuGlnSerPheLeuGluValSer TyrArqValLeuArqHisLeuAlaGlnProThrProLeuGlyProAlaSerSerLeuPro GlnSerPheLeuLeuLysSerLeuGluGlnValArgLysIleGlnGlyAspGlyAlaAla LeuGlnGluLysLeuCysAlaThrTyrLysLeuCysHisProGluGluLeuValLeuLeu GlyHisSerLeuGlyIleProTrpAlaProLeuSerSerCysProSerGlnAlaLeuGln LeuAlaGlyCysLeuSerGlnLeuHisSerGlyLeuPheLeuTyrGlnGlyLeuLeuGln AlaLeuGluGlyIleSerProGluLeuGlyProThrLeuAspThrLeuGlnLeuAspVal AlaAspPheAlaThrThrIleTrpGlnGlnMetGluGluLeuGlyMetAlaProAlaLeu GlnPro (SEQ ID NO:200);

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MetAlaAsnCysSerAsnMetIleAspGluIleIleThrHisLeuLysGlnProProLeuProLeuLeuAspPheAsnAsnLeuAsnGlyGluAspGlnAspIleLeuMetGluAsnAsn

LeuArgArgProAsnLeuGluAlaPheAsnArgAlaValLysSerLeuGlnAsnAlaSer AlaIleGluSerIleLeuLysAsnLeuLeuProCysLeuProLeuAlaThrAlaAlaPro ThrArgHisProIleIleIleArgAspGlyAspTrpAsnGluPheArgArgLysLeuThr PheTyrLeuLysThrLeuGluAsnAlaGlnAlaGlnGlnTyrValGluGlyGlyGlyGly SerProGlyGluProSerGlyProIleSerThrIleAsnProSerProProSerLysGlu SerHisLysSerProAsnMetAlaThrGlnGlyAlaMetProAlaPheAlaSerAlaPhe GlnArgArgAlaGlyGlyValLeuValAlaSerHisLeuGlnSerPheLeuGluValSer TyrArgValLeuArgHisLeuAlaGlnProSerGlyGlySerGlyGlySerGlnSerPhe LeuLeuLysSerLeuGluGlnValArgLysIleGlnGlyAspGlyAlaAlaLeuGlnGlu LysLeuCysAlaThrTyrLysLeuCysHisProGluGluLeuValLeuLeuGlyHisSer LeuGlyIleProTrpAlaProLeuSerSerCysProSerGlnAlaLeuGlnLeuAlaGly CysLeuSerGlnLeuHisSerGlyLeuPheLeuTyrGlnGlyLeuLeuGlnAlaLeuGlu GlyIleSerProGluLeuGlyProThrLeuAspThrLeuGlnLeuAspValAlaAspPhe AlaThrThrIleTrpGlnGlnMetGluGluLeuGlyMetAlaProAlaLeuGlnPro; (SEQ ID NO:201)

MetAlaAsnCysSerAsnMetIleAspGluIleIleThrHisLeuLysGlnProProLeu ProLeuLeuAspPheAsnAsnLeuAsnGlyGluAspGlnAspIleLeuMetAspAsnAsn LeuArgArgProAsnLeuGluAlaPheAsnArgAlaValLysSerLeuGlnAsnAlaSer AlaIleGluSerIleLeuLysAsnLeuLeuProCysLeuProLeuAlaThrAlaAlaPro ThrArqHisProIleHisIleLysAspGlyAspTrpAsnGluPheArqArqLysLeuThr PheTyrLeuLysThrLeuGluAsnAlaGlnAlaGlnGlnTyrValGluGlyGlyGlyGly SerProGlyGluProSerGlyProIleSerThrIleAsnProSerProProSerLysGlu SerHisLysSerProAsnMetAlaThrGlnGlyAlaMetProAlaPheAlaSerAlaPhe GlnArqArqAlaGlyGlyValLeuValAlaSerHisLeuGlnSerPheLeuGluValSer TyrArqValLeuArqHisLeuAlaGlnProThrProLeuGlyProAlaSerSerLeuPro GlnSerPheLeuLeuLysSerLeuGluGlnValArgLysIleGlnGlyAspGlyAlaAla LeuGlnGluLysLeuCysAlaThrTyrLysLeuCysHisProGluGluLeuValLeuLeu  ${\tt GlyHisSerLeuGlyIleProTrpAlaProLeuSerSerCysProSerGlnAlaLeuGln}$ LeuAlaGlyCysLeuSerGlnLeuHisSerGlyLeuPheLeuTyrGlnGlyLeuLeuGln AlaLeuGluGlyIleSerProGluLeuGlyProThrLeuAspThrLeuGlnLeuAspVal AlaAspPheAlaThrThrIleTrpGlnGlnMetGluGluLeuGlyMetAlaProAlaLeu GlnPro (SEQ ID NO:202);

AlaAsnCysSerIleMetIleAspGluIleIleHisHisLeuLysArgProProAlaPro LeuLeuAspProAsnAsnLeuAsnAspGluAspValSerIleLeuMetAspArgAsnLeu ArgLeuProAsnLeuGluSerPheValArgAlaValLysAsnLeuGluAsnAlaSerGly IleGluAlaIleLeuArgAsnLeuGlnProCysLeuProSerAlaThrAlaAlaProSer ArgHisProIleIleIleLysAlaGlyAspTrpGlnGluPheArgGluLysLeuThrPhe TyrLeuValThrLeuGluGlnAlaGlnGluGlnGlnTyrValGluGlyGlyGlyGlySer ProGlyGluProSerGlyProIleSerThrIleAsnProSerProProSerLysGluSer HisLysSerProAsnMetGlyProThrCysLeuSerSerLeuLeuGlyGlnLeuSerGly GlnValArgLeuLeuGlyAlaLeuGlnSerLeuLeuGlyThrGlnLeuProProGln GlyArgThrThrAlaHisLysAspProAsnAlaIlePheLeuSerPheGlnHisLeuLeu ArgGlyLysValArgPheLeuMetLeuValGlyGlySerThrLeuCysValArgGluPhe

GlyAsnMetAlaSerProAlaProProAlaCysAspLeuArgValLeuSerLysLeuLeu ArgAspSerHisValLeuHisSerArgLeuSerGlnCysProGluValHisProLeuPro ThrProValLeuLeuProAlaValAspPheSerLeuGlyGluTrpLysThrGlnMetGlu GluThrLysAlaGlnAspIleLeuGlyAlaValThrLeuLeuLeuGluGlyValMetAla AlaArgGlyGlnLeu (SEQ ID NO:221);

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AlaAsnCysSerIleMetIleAspGluIleIleHisHisLeuLysArgProProAlaPro LeuLeuAspProAsnAsnLeuAsnAspGluAspValSerIleLeuMetAspArgAsnLeu ArgLeuProAsnLeuGluSerPheValArgAlaValLysAsnLeuGluAsnAlaSerGly IleGluAlaIleLeuArgAsnLeuGlnProCysLeuProSerAlaThrAlaAlaProSer ArgHisProIleIleIleLysAlaGlyAspTrpGlnGluPheArgGluLysLeuThrPhe TyrLeuValThrLeuGluGlnAlaGlnGluGlnGlnTyrValGluGlyGlyGlyGlySer ProGlyGluProSerGlyProIleSerThrIleAsnProSerProProSerLysGluSer HisLysSerProAsnMetGlyThrGlnLeuProProGlnGlyArgThrThrAlaHisLys AspProAsnAlaIlePheLeuSerPheGlnHisLeuLeuArqGlyLysValArqPheLeu MetLeuValGlyGlySerThrLeuCysValArgGluPheGlyAsnMetAlaSerProAla ProProAlaCysAspLeuArqValLeuSerLysLeuLeuArqAspSerHisValLeuHis SerArgLeuSerGlnCysProGluValHisProLeuProThrProValLeuLeuProAla ValAspPheSerLeuGlyGluTrpLysThrGlnMetGluGluThrLysAlaGlnAspIle LeuGlyAlaValThrLeuLeuGluGlyValMetAlaAlaArqGlyGlnLeuGlyPro ThrCysLeuSerSerLeuLeuGlyGlnLeuSerGlyGlnValArgLeuLeuGlyAla LeuGlnSerLeuLeu (SEQ ID NO:222);

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AlaAsnCysSerIleMetIleAspGluIleIleHisHisLeuLysArgProProAlaPro LeuLeuAspProAsnAsnLeuAsnAspGluAspValSerIleLeuMetAspArqAsnLeu ArgLeuProAsnLeuGluSerPheValArgAlaValLysAsnLeuGluAsnAlaSerGly IleGluAlaIleLeuArqAsnLeuGlnProCysLeuProSerAlaThrAlaAlaProSer ArgHisProIleIleIleLysAlaGlyAspTrpGlnGluPheArgGluLysLeuThrPhe TyrLeuValThrLeuGluGlnAlaGlnGluGlnGlnTyrValGluGlyGlyGlyGlySer ProGlyGluProSerGlyProIleSerThrIleAsnProSerProProSerLysGluSer HisLysSerProAsnMetGlyProThrCysLeuSerSerLeuLeuGlyGlnLeuSerGly GlnValArgLeuLeuGlyAlaLeuGlnSerLeuLeuGlyThrGlnLeuProProGln GlyArgThrThrAlaHisLysAspProAsnAlaIlePheLeuSerPheGlnHisLeuLeu ArgGlyLysValArgPheLeuMetLeuValGlyGlySerThrLeuCysValArgGluPhe GlyGlyAsnGlyGlyAsnMetAlaSerProAlaProProAlaCysAspLeuArgValLeu SerLysLeuLeuArgAspSerHisValLeuHisSerArgLeuSerGlnCysProGluVal HisProLeuProThrProValLeuLeuProAlaValAspPheSerLeuGlyGluTrpLys ThrGlnMetGluGluThrLysAlaGlnAspIleLeuGlyAlaValThrLeuLeuGlu GlyValMetAlaAlaArgGlyGlnLeu (SEQ ID NO:223;

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AlaAsnCysSerIleMetIleAspGluIleIleHisHisLeuLysArgProProAlaPro LeuLeuAspProAsnAsnLeuAsnAspGluAspValSerIleLeuMetAspArgAsnLeu ArgLeuProAsnLeuGluSerPheValArgAlaValLysAsnLeuGluAsnAlaSerGly IleGluAlaIleLeuArgAsnLeuGlnProCysLeuProSerAlaThrAlaAlaProSer 847 ArgHisProIleIleIleLysAlaGlyAspTrpGlnGluPheArgGluLysLeuThrPhe 848 TyrLeuValThrLeuGluGlnAlaGlnGluGlnGlnTyrValGluGlyGlyGlyGlySer 849 ProGlyGluProSerGlyProIleSerThrIleAsnProSerProProSerLysGluSer 850 HisLysSerProAsnMetGlyThrGlnLeuProProGlnGlyArgThrThrAlaHisLys AspProAsnAlaIlePheLeuSerPheGlnHisLeuLeuArgGlyLysValArgPheLeu 851 852 MetLeuValGlyGlySerThrLeuCysValArgGluPheGlyGlyAsnGlyGlyAsnMet 853 AlaSerProAlaProProAlaCysAspLeuArgValLeuSerLysLeuLeuArgAspSer 854 HisValLeuHisSerArgLeuSerGlnCysProGluValHisProLeuProThrProVal 855 LeuLeuProAlaValAspPheSerLeuGlyGluTrpLysThrGlnMetGluGluThrLys 856 AlaGlnAspIleLeuGlyAlaValThrLeuLeuLeuGluGlyValMetAlaAlaArqGly 857 GlnLeuGlyProThrCysLeuSerSerLeuLeuGlyGlnLeuSerGlyGlnValArgLeu 858 LeuLeuGlyAlaLeuGlnSerLeuLeu (SEQ ID NO:234);

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AlaAsnCysSerIleMetIleAspGluIleIleHisHisLeuLysArgProProAlaPro LeuLeuAspProAsnAsnLeuAsnAspGluAspValSerIleLeuMetAspArgAsnLeu ArgLeuProAsnLeuGluSerPheValArgAlaValLysAsnLeuGluAsnAlaSerGly IleGluAlaIleLeuArqAsnLeuGlnProCysLeuProSerAlaThrAlaAlaProSer ArgHisProIleIleIleLysAlaGlyAspTrpGlnGluPheArgGluLysLeuThrPhe TyrLeuValThrLeuGluGlnAlaGlnGluGlnGlnTyrValGluGlyGlyGlyGlySer ProGlyGluProSerGlyProIleSerThrIleAsnProSerProProSerLysGluSer HisLysSerProAsnMetGlyArgThrThrAlaHisLysAspProAsnAlaIlePheLeu SerPheGlnHisLeuLeuArgGlyLysValArgPheLeuMetLeuValGlyGlySerThr LeuCysValArgGluPheGlyGlyAsnGlyGlyAsnMetAlaSerProAlaProProAla CysAspLeuArgValLeuSerLysLeuLeuArgAspSerHisValLeuHisSerArgLeu SerGlnCysProGluValHisProLeuProThrProValLeuLeuProAlaValAspPhe SerLeuGlyGluTrpLysThrGlnMetGluGluThrLysAlaGlnAspIleLeuGlyAla ValThrLeuLeuGluGlyValMetAlaAlaArgGlyGlnLeuGlyProThrCysLeu SerSerLeuLeuGlyGlnLeuSerGlyGlnValArqLeuLeuGlyAlaLeuGlnSer LeuLeuGlyThrGlnLeuProProGln (SEQ ID NO:235);

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AlaAsnCysSerIleMetIleAspGluIleIleHisHisLeuLysArgProProAlaPro
LeuLeuAspProAsnAsnLeuAsnAspGluAspValSerIleLeuMetAspArgAsnLeu
ArgLeuProAsnLeuGluSerPheValArgAlaValLysAsnLeuGluAsnAlaSerGly
IleGluAlaIleLeuArgAsnLeuGlnProCysLeuProSerAlaThrAlaAlaProSer
ArgHisProIleIleIleLysAlaGlyAspTrpGlnGluPheArgGluLysLeuThrPhe
TyrLeuValThrLeuGluGlnAlaGlnGluGlnGlnTyrValGluGlyGlyGlyGlySer
ProGlyGluProSerGlyProIleSerThrIleAsnProSerProProSerLysGluSer
HisLysSerProAsnMetAlaHisLysAspProAsnAlaIlePheLeuSerPheGlnHis
LeuLeuArgGlyLysValArgPheLeuMetLeuValGlyGlySerThrLeuCysValArg
GluPheGlyGlyAsnGlyGlyAsnMetAlaSerProAlaProProAlaCysAspLeuArg
ValLeuSerLysLeuLeuArgAspSerHisValLeuHisSerArgLeuSerGlnCysPro
GluValHisProLeuProThrProValLeuLeuProAlaValAspPheSerLeuGlyGlu
TrpLysThrGlnMetGluGluThrLysAlaGlnAspIleLeuGlyAlaValThrLeuLeu
LeuGluGlyValMetAlaAlaArgGlyGlnLeuGlyProThrCysLeuSerSerLeuLeu
GlyGlnLeuSerGlyGlnValArgLeuLeuLeuGlyAlaLeuGlnSerLeuLeuGlyThr

GlnLeuProProGlnGlyArgThrThr (SEQ ID NO:236);

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AlaAsnCysSerIleMetIleAspGluIleIleHisHisLeuLysArgProProAlaPro LeuLeuAspProAsnAsnLeuAsnAspGluAspValSerIleLeuMetAspArgAsnLeu ArgLeuProAsnLeuGluSerPheValArgAlaValLysAsnLeuGluAsnAlaSerGly IleGluAlaIleLeuArgAsnLeuGlnProCvsLeuProSerAlaThrAlaAlaProSer ArgHisProIleIleIleLysAlaGlyAspTrpGlnGluPheArgGluLysLeuThrPhe TyrLeuValThrLeuGluGlnAlaGlnGluGlnGlnTyrValGluGlyGlyGlySer ProGlyGluProSerGlyProIleSerThrIleAsnProSerProProSerLysGluSer HisLysSerProAsnMetAspProAsnAlaIlePheLeuSerPheGlnHisLeuLeuArg GlyLysValArgPheLeuMetLeuValGlyGlySerThrLeuCysValArgGluPheGly GlyAsnGlyGlyAsnMetAlaSerProAlaProProAlaCysAspLeuArgValLeuSer LysLeuLeuArgAspSerHisValLeuHisSerArgLeuSerGlnCysProGluValHis ProLeuProThrProValLeuLeuProAlaValAspPheSerLeuGlyGluTrpLysThr GlnMetGluGluThrLysAlaGlnAspIleLeuGlyAlaValThrLeuLeuLeuGluGly ValMetAlaAlaArqGlyGlnLeuGlyProThrCysLeuSerSerLeuLeuGlyGlnLeu SerGlyGlnValArqLeuLeuGlyAlaLeuGlnSerLeuLeuGlyThrGlnLeuPro ProGlnGlyArgThrThrAlaHisLys (SEQ ID NO:237);

913914915

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AlaAsnCysSerIleMetIleAspGluIleIleHisHisLeuLysArgProProAlaPro LeuLeuAspProAsnAsnLeuAsnAspGluAspValSerIleLeuMetAspArqAsnLeu ArgLeuProAsnLeuGluSerPheValArgAlaValLysAsnLeuGluAsnAlaSerGly IleGluAlaIleLeuArgAsnLeuGlnProCysLeuProSerAlaThrAlaAlaProSer ArgHisProIleIleIleLysAlaGlyAspTrpGlnGluPheArgGluLysLeuThrPhe TyrLeuValThrLeuGluGlnAlaGlnGluGlnGlnTyrValGluGlyGlyGlySer ProGlyGluProSerGlyProIleSerThrIleAsnProSerProProSerLysGluSer HisLysSerProAsnMetAlaIlePheLeuSerPheGlnHisLeuLeuArgGlvLysVal ArgPheLeuMetLeuValGlyGlySerThrLeuCysValArgGluPheGlyGlyAsnGly GlyAsnMetAlaSerProAlaProProAlaCysAspLeuArgValLeuSerLysLeuLeu ArgAspSerHisValLeuHisSerArgLeuSerGlnCysProGluValHisProLeuPro ThrProValLeuLeuProAlaValAspPheSerLeuGlyGluTrpLysThrGlnMetGlu GluThrLysAlaGlnAspIleLeuGlyAlaValThrLeuLeuGluGlyValMetAla AlaArgGlyGlnLeuGlyProThrCysLeuSerSerLeuLeuGlyGlnLeuSerGlyGln ValArgLeuLeuGlyAlaLeuGlnSerLeuLeuGlyThrGlnLeuProProGlnGly ArgThrThrAlaHisLysAspProAsn (SEQ ID NO:238);

931 932 933

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940

AlaAsnCysSerIleMetIleAspGluIleIleHisHisLeuLysArgProProAlaPro LeuLeuAspProAsnAsnLeuAsnAspGluAspValSerIleLeuMetAspArgAsnLeu ArgLeuProAsnLeuGluSerPheValArgAlaValLysAsnLeuGluAsnAlaSerGly IleGluAlaIleLeuArgAsnLeuGlnProCysLeuProSerAlaThrAlaAlaProSer ArgHisProIleIleIleLysAlaGlyAspTrpGlnGluPheArgGluLysLeuThrPhe TyrLeuValThrLeuGluGlnAlaGlnGluGlnGlnTyrValGluGlyGlyGlyGlySer ProGlyGluProSerGlyProIleSerThrIleAsnProSerProProSerLysGluSer HisLysSerProAsnMetAspProAsnAlaIlePheLeuSerPheGlnHisLeuLeuArg

941 GlyLysValArqPheLeuMetLeuValGlyGlySerThrLeuCysValArqGluPheGly 942 GlyAsnMetAlaSerProAlaProProAlaCysAspLeuArqValLeuSerLysLeuLeu 943 ArgAspSerHisValLeuHisSerArgLeuSerGlnCysProGluValHisProLeuPro 944 ThrProValLeuLeuProAlaValAspPheSerLeuGlyGluTrpLysThrGlnMetGlu 945 GluThrLysAlaGlnAspIleLeuGlyAlaValThrLeuLeuGluGlyValMetAla 946 AlaArqGlyGlnLeuGlyProThrCysLeuSerSerLeuLeuGlyGlnLeuSerGlyGln 947 ValArqLeuLeuGlyAlaLeuGlnSerLeuLeuGlyThrGlnGlyArqThrThrAla 948 HisLys (SEQ ID NO:239);

949

950 951

986

Leu

1 Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His 952 Leu 953 16 Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn 954 Asp 955 31 Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro 956 Asn 957 46 Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala 958 Ser 959 61 Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro 960 Ser 961 Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Lys Ala 76 962 Gly 963 91 Asp Trp Gln Glu Phe Arq Glu Lys Leu Thr Phe Tyr Leu Val 964 Thr 965 106 Leu Glu Gln Ala Gln Glu Gln Tyr Val Glu Gly Gly 966 Gly 967 121 Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro 968 Ser 969 136 Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Leu 970 Gly 971 151 Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Lys Ser Leu 972 Glu 973 166 Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu 974 Lys 975 181 Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val 976 Leu 977 196 Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser 978 Cys 979 211 Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu 980 His 981 226 Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu 982 Gly 983 241 Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu 984 Asp 985 256 Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu

```
987
       271
            Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro
988
      Ala
989
       286
            Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val
990
      Ala
991
       301
            Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu
992
      Arg
993
       316
            His Leu Ala Gln Pro Asp Met Ala Thr Pro (SEQ ID NO:271);
994
995
996
         1
            Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
997
      Leu
998
            Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn
        16
      Asp
999
1000
        31
            Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro
1001
      Asn
1002
        46
            Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala
1003
      Ser
1004
            Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro
        61
1005
      Ser
1006
        76
            Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Lys Ala
1007
      Gly
1008
        31
            Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val
1009
      Thr
1010
       106
            Leu Glu Gln Ala Gln Glu Gln Tyr Val Glu Gly Gly
1011
      Gly
1012
       121
            Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro
1013
      Ser
            Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Leu
1014
       136
1015
      Gly
            Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Ser Leu
1016
       151
1017
      Glu
1018
       176
            Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu
1019
      Lys
1020
       191
            Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val
1021
      Leu
1022
       206
            Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
1023
      Cys
1024
       221
            Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu
1025
      His
1026
       236
            Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu
1027
      Gly
1028
       251
            Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu
1029
      Asp
1030
       266
            Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu
1031
      Leu
1032
       281
            Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro
1033
      Ala
```

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1034
       296
            Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val
1035
      Ala
1036
       311
            Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu
1037
      Arq
1038
       326
            His Leu Ala Gln Pro Asp Met Ala Thr Pro (SEQ ID NO:272);
1039
1040
1041
         1
            Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
1042
      Leu
1043
        16
            Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn
1044
      Asp
1045
        31
            Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro
1046
      Asn
1047
        46
            Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala
1048
      Ser
1049
            Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro
        61
1050
      Ser
1051
        76
            Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Lys Ala
1052
      Gly
1053
        91
            Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val
1054
      Thr
1055
       106
            Leu Glu Gln Ala Gln Glu Gln Tyr Val Glu Gly Gly Gly
1056
      Gly
1057
       121
            Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro
1058
      Ser
1059
       136
            Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Phe
1060
      Leu
1061
       151
            Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly
1062
      Ala
1063
       166
            Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His
1064
      Pro
1065
       181
            Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp
1066
      Ala
1067
       196
            Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly
1068
      Cys
1069
       211
            Leu Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu
1070
      Leu
1071
       226
            Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu
1072
      Asp
1073
       241
            Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp
1074
      Gln
1075
       256
            Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro Thr
1076
      Gln
1077
       271
            Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala
1078
      Gly
1079
       286
            Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu Val
1080
      Ser
```

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1081
            Tyr Arg Val Leu Arg His Leu Ala Gln Pro Asp Met Ala Thr
       301
1082
      Pro
1083
            Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser (SEQ ID NO:273);
       316
1084
1085
1086
         1
            Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
1087
      Leu
1088
            Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn
        16
1089
      Asp
1090
        31
            Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro
1091
      Asn
1092
        46
            Leu Glu Ser Phe Val Arq Ala Val Lys Asn Leu Glu Asn Ala
1093
      Ser
1094
        61
            Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro
1095
      Ser
1096
        76
            Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Lys Ala
1097
      Gly
1098
        91
            Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val
1099
      Thr
1100
            Leu Glu Gln Ala Gln Glu Gln Tyr Val Glu Gly Gly
       106
1101
      Gly
       121
1102
            Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro
      Ser
1103
1104
       136
            Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Glu
1105
      Gln
1106
       151
            Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys
1107
      Leu
1108
       166
            Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu
1109
      Leu
1110
       181
            Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys
1111
      Pro
1112
       196
            Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
1113
      Ser
1114
       211
            Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly
1115
      Ile
1116
       226
            Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp
1117
      Val
1118
            Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu
       241
1119
      Gly
1120
       256
            Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala
1121
      Phe
1122
            Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala
       271
      Ser
1123
1124
       286
            His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg
1125
      His
1126
       301
            Leu Ala Gln Pro Asp Met Ala Thr Pro Leu Gly Pro Ala Ser
1127
      Ser
```

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1128
            Leu Pro Gln Ser Phe Leu Leu Lys Ser Leu (SEQ ID NO:274);
       316
1129
1130
1131
            Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
         1
1132
      Leu
1133
            Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn
        16
1134
      Asp
1135
        31
            Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro
1136
      Asn
1137
            Leu Glu Ser Phe Val Arq Ala Val Lys Asn Leu Glu Asn Ala
        46
1138
      Ser
1139
        61
            Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro
1140
      Ser
1141
        76
            Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Lys Ala
1142
      Gly
1143
            Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val
        91
1144
      Thr
1145
       106
            Leu Glu Gln Ala Gln Glu Gln Tyr Val Glu Gly Gly
1146
      Gly
1147
       121
            Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro
1148
      Ser
1149
       136
            Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Leu
1150
      Leu
1151
       151
            Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys
1152
      Pro
1153
       166
            Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
1154
      Ser
1155
       181
            Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly
1156
      Ile
1157
            Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp
       196
1158
      Val
            Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu
1159
       211
1160
      Gly
1161
       226
            Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala
1162
      Phe
1163
       241
            Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala
1164
      Ser
1165
       256
            His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arq Val Leu Arq
1166
      His
            Leu Ala Gln Pro Asp Met Ala Thr Pro Leu Gly Pro Ala Ser
1167
       271
1168
      Ser
1169
       286
            Leu Pro Gln Ser Phe Leu Leu Lys Ser Leu Glu Gln Val Arg
1170
      Lys
1171
       301
            Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala
1172
      Thr
1173
       316
            Tyr Lys Leu Cys His Pro Glu Glu Leu Val (SEQ ID NO:275);
1174
```

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1175
1176
         1
            Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
1177
      Leu
1178
            Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn
        16
1179
     Asp
            Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro
1180
        31
1181
      Asn
1182
        46
            Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala
1183
      Ser
1184
            Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro
        61
1185
      Ser
1186
        76
            Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Lys Ala
1187
      Gly
1188
        91
            Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val
1189
      Thr
1190
            Leu Glu Gln Ala Gln Glu Gln Tyr Val Glu Gly Gly
       106
1191
      Gly
1192
       121
            Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro
1193
      Ser
1194
       136
            Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Pro
1195
      Leu
1196
       151
            Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu
1197
      Ser
1198
       166
            Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln
1199
      Ala
1200
       181
            Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr
     Leu
1201
1202
       196
            Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln
1203
      Met
1204
       211
            Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly
1205
      Ala
1206
       226
            Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly
1207
      Val
1208
       241
            Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr
1209
     Arq
1210
       256
            Val Leu Arg His Leu Ala Gln Pro Asp Met Ala Thr Pro Leu
1211
      Gly
1212
      271
            Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Lys Ser Leu
1213
      Glu
1214
      286
            Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu
1215
      Lys
1216
       301
            Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val
1217
      Leu
1218
       316
            Leu Gly His Ser Leu Gly Ile Pro Trp Ala (SEQ ID NO:276);
1219
1220
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1221
            Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
         1
1222
      Leu
1223
        16
            Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn
1224
      Asp
1225
        31
            Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro
1226
      Asn
1227
        46
            Leu Glu Ser Phe Val Arq Ala Val Lys Asn Leu Glu Asn Ala
1228
      Ser
1229
        61
            Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro
1230
      Ser
1231
        76
            Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Lys Ala
1232
      Gly
1233
            Asp Trp Gln Glu Phe Arq Glu Lys Leu Thr Phe Tyr Leu Val
        91
1234
      Thr
1235
       106
            Leu Glu Gln Ala Gln Glu Gln Tyr Val Glu Gly Gly
1236
      Gly
1237
       121
            Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro
1238
      Ser
1239
       136
            Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Gln
1240
      Ala
1241
       151
            Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu
1242
      Phe
1243
       166
            Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser Pro
1244
      Glu
1245
       181
            Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp
1246
      Phe
1247
       196
            Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
1248
      Pro
1249
            Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser
       211
1250
      Ala
1251
       226
            Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu
1252
      Gln
1253
       241
            Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala
1254
      Gln
1255
       256
            Pro Asp Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro
1256
      Gln
1257
       271
            Ser Phe Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln
1258
      Gly
1259
       286
            Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys
1260
      Leu
1261
       301
            Cys His Pro Glu Glu Leu Val Leu Gly His Ser Leu Gly
1262
      Ile
1263
       316
            Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser (SEQ ID NO:277);
1264
1265
1266
         1
            Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
1267
     Leu
```

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1268
        16
            Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn
1269
      Asp
1270
        31
            Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro
1271
      Asn
1272
            Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala
        46
1273
      Ser
1274
        61
            Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro
1275
      Ser
1276
        76
            Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Lys Ala
1277
      Gly
1278
        91
            Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val
1279
      Thr
1280
       106
            Leu Glu Gln Ala Gln Glu Gln Tyr Val Glu Gly Gly Gly
1281
      Gly
1282
       121
            Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro
1283
      Ser
1284
       136
            Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Leu
1285
      Gln
1286
       151
            Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu Phe Leu
1287
      Tyr
1288
       166
            Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu
1289
      Gly
1290
            Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala
       181
1291
      Thr
1292
       196
            Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala
1293
      Leu
1294
       211
            Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe
1295
      Gln
1296
       226
            Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
1297
      Phe
1298
       241
            Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
1299
      Asp
1300
       256
            Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser
1301
      Phe
1302
            Leu Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp
       271
1303
      Gly
1304
       286
            Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys
1305
      His
1306
       301
            Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro
1307
      Trp
1308
       316
            Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala (SEQ ID NO:278);
1309
1310
1311
         1
            Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
1312
      Leu
1313
        16
            Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn
1314
      Asp
```

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1315
            Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro
        31
1316
      Asn
1317
        46
            Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala
1318
      Ser
1319
        61
            Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro
1320
      Ser
1321
        76
            Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Lys Ala
1322
      Gly
1323
        91
            Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val
1324
      Thr
1325
       106
            Leu Glu Gln Ala Gln Glu Gln Tyr Val Glu Gly Gly
1326
      Gly
1327
       121
            Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro
1328
      Ser
1329
       136
            Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Leu
1330
      Ala
1331
       151
            Gly Cys Leu Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln
1332
      Gly
1333
       166
            Leu Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro
1334
      Thr
1335
       181
            Leu Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr
1336
      Ile
1337
       196
            Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln
1338
      Pro
1339
            Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg
       211
1340
      Arq
1341
       226
            Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu
1342
      Glu
1343
       241
            Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro Asp Met
1344
      Ala
1345
       256
            Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu
1346
      Leu
1347
       271
            Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala
1348
      Ala
1349
       286
            Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro
1350
      Glu
1351
       301
            Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala
1352
      Pro
1353
       316
            Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln (SEQ ID NO:279);
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1355
1356
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     Leu
1358
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            Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn
1359
      Asp
1360
        31
            Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro
1361
      Asn
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1362
        46
1363
      Ser
1364
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        61
1365
      Ser
1366
        76
            Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Lys Ala
1367
      Gly
1368
        91
            Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val
1369
      Thr
1370
       106
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1371
      Gly
1372
       121
            Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro
1373
      Ser
1374
       136
            Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Glu
1375
      Leu
1376
       151
            Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro
1377
      Ala
1378
            Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val
       166
1379
      Ala
1380
       181
            Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arq Val Leu
1381
      Arq
1382
       196
            His Leu Ala Gln Pro Asp Met Ala Thr Pro Leu Gly Pro Ala
1383
      Ser
1384
       211
            Ser Leu Pro Gln Ser Phe Leu Leu Lys Ser Leu Glu Gln Val
1385
      Arg
1386
       226
            Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys
1387
      Ala
1388
       241
            Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly
1389
      His
1390
       256
            Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser
1391
      Gln
1392
       271
            Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly
1393
      Leu
1394
       286
            Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser
1395
      Pro
1396
       301
            Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
1397
      Asp
1398
       316
            Phe Ala Thr Thr Ile Trp Gln Gln Met Glu (SEQ ID NO:280);
1399
1400
1401
         1
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1402
      Leu
1403
        16
            Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn
1404
      Asp
1405
        31
            Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro
1406
      Asn
1407
        46
            Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala
1408
      Ser
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1409
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1410
      Ser
1411
            Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Lys Ala
        76
1412
      Gly
1413
        91
            Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val
1414
      Thr
1415
            Leu Glu Gln Ala Gln Glu Gln Tyr Val Glu Gly Gly Gly
       106
1416
      Gly
1417
       121
            Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro
1418
      Ser
1419
       136
            Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Gly
1420
      Met
1421
            Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe
       151
1422
      Ala
1423
       166
            Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser
1424
      His
1425
            Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His
       181
1426
      Leu
1427
       196
            Ala Gln Pro Asp Met Ala Thr Pro Leu Gly Pro Ala Ser Ser
1428
      Leu
1429
       211
            Pro Gln Ser Phe Leu Leu Lys Ser Leu Glu Gln Val Arg Lys
1430
      Ile
1431
       226
            Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr
1432
      Tyr
1433
       241
            Lys Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His Ser
1434
      Leu
1435
       256
            Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala
1436
      Leu
1437
       271
            Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu Phe
1438
      Leu
1439
       286
            Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu
1440
      Leu
1441
            Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp Phe
       301
      Ala
1442
1443
       316
            Thr Thr Ile Trp Gln Gln Met Glu Glu Leu (SEQ ID NO:281);
1444
      and
1445
1446
1447
            Met Ala Asn Cys Ser Ile Met Ile Asp Glu Ile Ile His His
         1
1448
      Leu
1449
            Lys Arg Pro Pro Ala Pro Leu Leu Asp Pro Asn Asn Leu Asn
        16
1450
      Asp
            Glu Asp Val Ser Ile Leu Met Asp Arg Asn Leu Arg Leu Pro
1451
        31
1452
      Asn
1453
            Leu Glu Ser Phe Val Arg Ala Val Lys Asn Leu Glu Asn Ala
        46
1454
      Ser
```

Gly Ile Glu Ala Ile Leu Arg Asn Leu Gln Pro Cys Leu Pro Ser Ala Thr Ala Ala Pro Ser Arg His Pro Ile Ile Lys Ala Gly Asp Trp Gln Glu Phe Arg Glu Lys Leu Thr Phe Tyr Leu Val Thr Leu Glu Gln Ala Gln Glu Gln Tyr Val Glu Gly Gly Gly Ser Pro Gly Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn Pro Ser Pro Pro Ser Lys Glu Ser His Lys Ser Pro Asn Met Ala Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro Asp Met Ala Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Ser Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln (SEQ ID NO:282).

16. The hematopoeitic protein as recieted in claim 1 wherein said c-mpl receptor agonist is selected from the group consisiting of:

MetAlaGlyArgThrThrAlaHisLysAspProAsnAlaIlePheLeuSerPheGlnHis LeuLeuArgGlyLysValArgPheLeuMetLeuValGlyGlySerThrLeuAlaValArg GluPheGlyGlyAsnMetAlaSerProAlaProProAlaAlaAspLeuArgValLeuSer LysLeuLeuArgAspSerHisValLeuHisSerArgLeuSerGlnCysProGluValHis ProLeuProThrProValLeuLeuProAlaValAspPheSerLeuGlyGluTrpLysThr GlnMetGluGluThrLysAlaGlnAspIleLeuGlyAlaValThrLeuLeuLeuGluGly ValMetAlaAlaArgGlyGlnLeuGlyProThrCysLeuSerSerLeuLeuGlyGlnLeu

- 12 SerGlyGlnValArgLeuLeuGlyAlaLeuGlnSerLeuLeuGlyThrGlnLeuPro
- 13 ProGln (SEQ ID NO:284); and

- 15 MetAlaGlyProThrCysLeuSerSerLeuLeuGlyGlnLeuSerGlyGlnValArgLeu
- 16 LeuLeuGlyAlaLeuGlnSerLeuLeuGlyThrGlnLeuProProGlnGlyArgThrThr
- 17 AlaHisLysAspProAsnAlaIlePheLeuSerPheGlnHisLeuLeuArgGlyLysVal
- 18 ArgPheLeuMetLeuValGlyGlySerThrLeuAlaValArgGluPheGlyGlyAsnMet
- 19 AlaSerProAlaProProAlaAlaAspLeuArgValLeuSerLysLeuLeuArgAspSer
- 20 HisValLeuHisSerArgLeuSerGlnCysProGluValHisProLeuProThrProVal
- 21 LeuLeuProAlaValAspPheSerLeuGlyGluTrpLysThrGlnMetGluGluThrLys
- 22 AlaGlnAspIleLeuGlyAlaValThrLeuLeuLeuGluGlyValMetAlaAlaArgGly
- 23 GlnLeu (SEQ ID NO:285)
- 1 17. The hematopoietic protein of claim 1, 2, 3, 4, 5, 6,
- 2 7, 8, 9, 10, 11 or 12 wherein said colony stimulating factor
- 3 is selected from the group consisting of GM-CSF, G-CSF, G-CSF
- 4 Ser $^{17}$ , c-mpl ligand (TPO), M-CSF, erythropoietin (EPO), IL-1,
- 5 IL-4, IL-2, IL-3, IL-5, IL 6, IL-7, IL-8, IL-9, IL-10, IL-11,
- 6 IL-12, IL-13, IL-15, LIF, flt3/flk2 ligand, human growth
- 7 hormone, B-cell growth factor, B-cell differentiation factor,
- 8 eosinophil differentiation factor and stem cell factor (SCF).
- 1 18. The hematopoietic protein of claim 17 wherein said
- 2 colony stimulating factor is selected from the group
- 3 consisting of G-CSF, G-CSF  $Ser^{17}$  and c-mpl ligand (TPO).
- 1 19. A nucleic acid molecule encoding said hematopoietic
- 2 protein of claim 1.
- 1 20. A nucleic acid molecule encoding said hematopoietic
- 2 protein of claim 2.
- 1 21. A nucleic acid molecule encoding said hematopoietic
- 2 protein of claim 3.
- 1 22. A nucleic acid molecule encoding said hematopoietic
- 2 protein of claim 4.

- 1 23. A nucleic acid molecule encoding said hematopoietic
- 2 protein of claim 5.
- 1 24. A nucleic acid molecule encoding said hematopoietic
- 2 protein of claim 6.
- 1 25. A nucleic acid molecule encoding said hematopoietic
- 2 protein of claim 7.
- 1 26. A nucleic acid molecule encoding said hematopoietic
- 2 protein of claim 8.
- 1 27. A nucleic acid molecule encoding said hematopoietic
- 2 protein of claim 9.
- 1 28. A nucleic acid molecule encoding said hematopoietic
- 2 protein of claim 10.
- 1 29. A nucleic acid molecule encoding said hematopoietic
- 2 protein of claim 11.
- 1 30. A nucleic acid molecule encoding said hematopoietic
- 2 protein of claim 12.
- 1 31. A nucleic acid molecule encoding said hematopoietic
- 2 protein of claim 13.
- 1 32. A nucleic acid molecule encoding said hematopoietic
- 2 protein of claim 14.
- 1 33. A nucleic acid molecule encoding said hematopoietic
- 2 protein of claim 15.
- 1 34. A nucleic acid molecule encoding said hematopoietic
- 2 protein of claim 16.

1 35. A nucleic acid molecule encoding said hematopoietic 2 protein of claim 17.

```
1
         36.
              The nucleic acid molecule according to claim 30
2
    selected from group consisting of:
3
4
5
      1
         ATGGCTAACT GCTCTATAAT GATCGATGAA ATTATACATC ACTTAAAGAG
6
     51
         ACCACCTGCA CCTTTGCTGG ACCCGAACAA CCTCAATGAC GAAGACGTCT
7
    101
         CTATCCTGAT GGACCGAAAC CTTCGACTTC CAAACCTGGA GAGCTTCGTA
8
    151
         AGGGCTGTCA AGAACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
         TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC TCTCGACATC
9
    201
10
    251
         CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG
11
    301
         TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAGAGGG
         CGGTGGAGGC TCCCCGGGTG GTGGTTCTGG CGGCGGCTCC AACATGGCTT
12
    351
13
    401
         ACAAGCTGTG CCACCCCGAG GAGCTGGTGC TGCTCGGACA CTCTCTGGGC
14
    451
         ATCCCCTGGG CTCCCTGAG CTCCTGCCC AGCCAGGCCC TGCAGCTGGC
15
    501
         AGGCTGCTTG AGCCAACTCC ATAGCGGCCT TTTCCTCTAC CAGGGGCTCC
16
    551
         TGCAGGCCCT GGAAGGGATA TCCCCCGAGT TGGGTCCCAC CTTGGACACA
17
    601
         CTGCAGCTGG ACGTCGCCGA CTTTGCCACC ACCATCTGGC AGCAGATGGA
18
    651
         AGAACTGGGA ATGGCCCCTG CCCTGCAGCC CACCCAGGGT GCCATGCCGG
19
    701
         CCTTCGCCTC TGCTTTCCAG CGCCGGGCAG GAGGGGTCCT GGTTGCTAGC
20
    751
         CATCTGCAGA GCTTCCTGGA GGTGTCGTAC CGCGTTCTAC GCCACCTTGC
21
    801
         GCAGCCCTCT GGCGGCTCTG GCGGCTCTCA GAGCTTCCTG CTCAAGTCTT
22
    851
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23
    901
         CTGTGTGCCA CCTAATAA (SEQ ID NO:94);
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25
26
      1
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27
     51
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28
    101
         CTATCCTGAT GGACCGAAAC CTTCGACTTC CAAACCTGGA GAGCTTCGTA
29
         AGGGCTGTCA AGAACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
    151
30
    201
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31
    251
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32
    301
         TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAGAGGG
33
    351
         CGGTGGAGGC TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC
34
    401
         CGTCTCCTCC GTCTAAAGAA TCTCATAAAT CTCCAAACAT GGCTTACAAG
35
    451
         CTGTGCCACC CCGAGGAGCT GGTGCTGCTC GGACACTCTC TGGGCATCCC
36
    501
         CTGGGCTCCC CTGAGCTCCT GCCCCAGCCA GGCCCTGCAG CTGGCAGGCT
37
    551
         GCTTGAGCCA ACTCCATAGC GGCCTTTTCC TCTACCAGGG GCTCCTGCAG
38
    601
         GCCCTGGAAG GGATATCCCC CGAGTTGGGT CCCACCTTGG ACACACTGCA
39
    651
         GCTGGACGTC GCCGACTTTG CCACCACCAT CTGGCAGCAG ATGGAAGAAC
40
         TGGGAATGGC CCCTGCCCTG CAGCCCACCC AGGGTGCCAT GCCGGCCTTC
    701
41
    751
         GCCTCTGCTT TCCAGCGCCG GGCAGGAGGG GTCCTGGTTG CTAGCCATCT
42
    801
         GCAGAGCTTC CTGGAGGTGT CGTACCGCGT TCTACGCCAC CTTGCGCAGC
43
    851
         CCTCTGGCGG CTCTGGCGGC TCTCAGAGCT TCCTGCTCAA GTCTTTAGAG
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44
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45
    951
         TGCCACCTAA TAA (SEQ ID NO:95);
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47
48
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49
     51
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50
    101
         CTATCCTGAT GGACCGAAAC CTTCGACTTC CAAACCTGGA GAGCTTCGTA
51
    151
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52
    201
         TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC TCTCGACATC
53
    251
         CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG
54
    301
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55
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56
    401
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         GCCACCACCA TCTGGCAGCA GATGGAAGAA CTGGGAATGG CCCCTGCCCT
57
    451
58
    501
         GCAGCCCACC CAGGGTGCCA TGCCGGCCTT CGCCTCTGCT TTCCAGCGCC
59
    551
         GGGCAGGAGG GGTCCTGGTT GCTAGCCATC TGCAGAGCTT CCTGGAGGTG
60
    601
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61
    651
         CTCTCAGAGC TTCCTGCTCA AGTCTTTAGA GCAAGTGAGA AAGATCCAGG
62
    701
         GCGATGCCC AGCGCTCCAG GAGAAGCTGT GTGCCACCTA CAAGCTGTGC
63
    751
         CACCCGAGG AGCTGGTGCT GCTCGGACAC TCTCTGGGCA TCCCCTGGGC
64
    801
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         GCCAACTCCA TAGCGGCCTT TTCCTCTACC AGGGGCTCCT GCAGGCCCTG
65
    851
66
    901
         GAAGGGATAT CCTAATAA (SEQ ID NO:96);
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68
69
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      1
70
     51
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71
    101
         CTATCCTGAT GGACCGAAAC CTTCGACTTC CAAACCTGGA GAGCTTCGTA
72
         AGGGCTGTCA AGAACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
    151
73
    201
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74
    251
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75
         TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAGAGGG
    301
76
    351
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77
    401
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78
    451
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79
    501
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         CCACCCAGGG TGCCATGCCG GCCTTCGCCT CTGCTTTCCA GCGCCGGGCA
80
    551
81
    601
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82
         CCGCGTTCTA CGCCACCTTG CGCAGCCCTC TGGCGGCTCT GGCGGCTCTC
    651
83
         AGAGCTTCCT GCTCAAGTCT TTAGAGCAAG TGAGAAAGAT CCAGGGCGAT
    701
84
    751
         GGCGCAGCGC TCCAGGAGAA GCTGTGTGCC ACCTACAAGC TGTGCCACCC
85
         CGAGGAGCTG GTGCTGCTCG GACACTCTCT GGGCATCCCC TGGGCTCCCC
    801
86
    851
         TGAGCTCCTG CCCCAGCCAG GCCCTGCAGC TGGCAGGCTG CTTGAGCCAA
87
    901
         CTCCATAGCG GCCTTTTCCT CTACCAGGGG CTCCTGCAGG CCCTGGAAGG
88
    951
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89
90
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93
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94
     151
         AGGGCTGTCA AGAACTTAGA AAATGCATCA GGTATTGAGG CAATTCTTCG
95
     201
          TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC TCTCGACATC
          CAATCATCAT CAAGGCAGGT GACTGGCAAG AATTCCGGGA AAAACTGACG
96
    251
97
     301
          TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAGAGGG
98
     351
          CGGTGGAGGC TCCCCGGGTG GTGGTTCTGG CGCCGGCTCC AACATGGCTA
99
     401
          TGGCCCCTGC CCTGCAGCCC ACCCAGGGTG CCATGCCGGC CTTCGCCTCT
100
     451
          GCTTTCCAGC GCCGGGCAGG AGGGGTCCTG GTTGCTAGCC ATCTGCAGAG
101
     501
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102
          GCGGCTCTGG CGGCTCTCAG AGCTTCCTGC TCAAGTCTTT AGAGCAAGTG
     551
103
     601
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104
     651
          CTACAAGCTG TGCCACCCCG AGGAGCTGGT GCTGCTCGGA CACTCTCTGG
105
     701
          GCATCCCCTG GGCTCCCCTG AGCTCCTGCC CCAGCCAGGC CCTGCAGCTG
106
     751
          GCAGGCTGCT TGAGCCAACT CCATAGCGGC CTTTTCCTCT ACCAGGGGCT
107
     801
          CCTGCAGGCC CTGGAAGGGA TATCCCCCGA GTTGGGTCCC ACCTTGGACA
108
     851
          CACTGCAGCT GGACGTCGCC GACTTTGCCA CCACCATCTG GCAGCAGATG
109
     901
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112
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114
     101
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115
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116
     201
117
     251
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118
     301
          TTCTATCTGG TTACCCTTGA GCAAGCGCAG GAACAACAGT ACGTAGAGGG
119
     351
         CGGTGGAGGC TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC
120
     401
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121
     451
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122
     501
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125
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     651
126
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127
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128
     801
          CTGCTTGAGC CAACTCCATA GCGGCCTTTT CCTCTACCAG GGGCTCCTGC
129
     851
          AGGCCCTGGA AGGGATATCC CCCGAGTTGG GTCCCACCTT GGACACACTG
130
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134
       1
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136
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      951
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988
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989
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1140
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1141
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       601
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1148
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1149
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1161
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       601
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       651
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            CCAGGCCCTG CAGCTGGCAG GCTGCTTGAG CCAACTCCAT AGCGGCCTTT
1173
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1174
       851
            TCCTCTACCA GGGGCTCCTG CAGGCCCTGG AAGGGATATC CCCCGAGTTG
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       901
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            CATCTGGCAG CAGATGGAAG AACTG (SEQ ID NO:269); and
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1179
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            ACCACCTGCA CCTTTGCTGG ACCCGAACAA CCTCAATGAC GAAGACGTCT
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       101
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1182
       151
1183
       201
            TAATCTCCAA CCATGTCTGC CCTCTGCCAC GGCCGCACCC TCTCGACATC
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       251
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1185
       301
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            CGGTGGAGGC TCCCCGGGTG AACCGTCTGG TCCAATCTCT ACTATCAACC
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1192
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1193
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1194
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1195
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1196
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1197
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1198
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37. The nucleic acid molecule according to claim 34 selected from group consisting of:

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     201
9
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          TACACCTGTC CTGCTGCCTG CTGTGGACTT TAGCTTGGGA GAATGGAAAA
     351
12
     401
          CCCAGATGGA GGAGACCAAG GCACAGGACA TTCTGGGAGC AGTGACCCTT
13
     451
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14
         (SEO ID NO:286); and
15
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16 1 ATGGCTGGCA GGACCACAGC TCACAAGGAT CCCAATGCCA TCTTCCTGAG
17 51 CTTCCAACAC CTGCTCCGAG GAAAGGTGCG TTTCCTGATG CTTGTAGGAG
18 101 GGTCCACCCT CGCCGTCAGG GAATTCGGCG GCAACATGGC GTCTCCGGCG

- 19 151 CCGCCTGCTG CTGACCTCCG AGTCCTCAGT AAACTGCTTC GTGACTCCCA
- 20 201 TGTCCTTCAC AGCAGACTGA GCCAGTGCCC AGAGGTTCAC CCTTTGCCTA
- 21 251 CACCTGTCCT GCTGCCTGCT GTGGACTTTA GCTTGGGAGA ATGGAAAACC
- 22 301 CAGATGGAGG AGACCAAGGC ACAGGACATT CTGGGAGCAG TGACCCTTCT
- 23 351 GCTGGAGGA GTGATGGCAG CACGGGGACA ACTGGGACCC ACTTGCCTCT
- 24 401 CATCCCTCCT GGGGCAGCTT TCTGGACAGG TCCGTCTCCT CCTTGGGGCC
- 25 451 CTGCAGAGCC TCCTTGGAAC CCAGCTTCCT CCACAG
- 26 (SEQ ID NO:287).
- 1 38. A method of producing a hematopoietic protein
- 2 comprising: growing under suitable nutrient conditions, a host
- 3 cell transformed or transfected with a replicable vector
- 4 comprising a nucleic acid molecule of claim 20, 21, 22, 23,
- 5 24, 25, 26, 27, 28, 30, 33, 34, 36 or 37 in a manner allowing
- 6 expression of said hematopoietic protein and recovering said
- 7 hematopoietic protein.
- 1 39. A pharmaceutical composition comprising; the
- 2 hematopoietic protein according to claim 1, 2, 3, 4, 5, 6, 7,
- 3 8, 9, 10, 12, 15 or 16 and a pharmaceutically acceptable
- 4 carrier.
- 1 40. A method of stimulating the production of
- 2 hematopoietic cells in a patient comprising the step of;
- 3 administering an effective amount of the hematopoietic protein
- 4 as recited in claim 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 15, or
- 5 16 to said patient.
- 1 41. A method of stimulating the production of
- 2 hematopoietic cells in a patient comprising the step of
- 3 administering an effective amount of the hematopoietic protein
- 4 as recited in claim 13 to said patient.
- 1 42. A method for selective ex vivo expansion of stem
- 2 cells, comprising the steps of:
- 3 (a) separating stem cells from other cells;

4 (b) culturing said separated stem cells with a selected 5 culture medium comprising; the hematopoietic protein of claim 6 1; and 7 (c) harvesting said cultured cells. 1 A method for treatment of a patient having a 2 hematopoietic disorder, comprising the steps of: 3 (a) removing stem cells; (b) separating stem cells from other cells; 5 (c) culturing said separated stem cells with a selected 6 culture medium comprising; the hematopoietic protein of claim 7 1; 8 (d) harvesting said cultured cells; and 9 (e) transplanting said cultured cells into said patient. 1 44. A method of human gene therapy, comprising the steps 2 of: 3 (a) removing stem cells from a patient; (b) separating said stem cells from other cells; 5 (c) culturing said separated stem cells with a selected 6 culture medium comprising; the hematopoietic protein of claim 7 1; 8 (d) introducing DNA into said cultured cells; 9 (e) harvesting said transduced cells; and 10 (f) transplanting said transduced cells into said 11 patient. 1 A method of human gene therapy, comprising the steps 45. of: 2 3 (a) removing stem cells from a patient; 4 (b) separating said stem cells from other cells; 5 (c) culturing said separated stem cells with a selected 6 culture medium comprising; the hematopoietic protein of claim 7 1: 8 (d) introducing DNA into said cultured cells;

(e) harvesting said transduced cells; and

(f) transplanting said transduced cells into said 11 patient. 1 A method of human gene therapy, comprising the steps 46. 2 of: 3 (a) removing stem cells from a patient; 4 (b) separating said stem cells from other cells; 5 (c) culturing said separated stem cells with a selected 6 culture medium comprising; the hematopoietic protein of claim 7 11; 8 (d) introducing DNA into said cultured cells; 9 (e) harvesting said transduced cells; and 10 (f) transplanting said transduced cells into said 11 patient. 1 . A method of human gene therapy, comprising the steps 47. 2 of: 3 (a) removing stem cells from a patient; 4 (b) separating said stem cells from other cells; 5 (c) culturing said separated stem cells with a selected 6 culture medium comprising; the hematopoietic protein of claim 7 11; 8 (d) introducing DNA into said cultured cells; 9 (e) harvesting said transduced cells; and 10 (f) transplanting said transduced cells into said 11 patient.